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# UNITED STATES NAVY MEDICAL NEWS LETTER

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*MEDICAL NEWS LETTER*
*United States Navy*

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### *Policy*

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

### *Change of Address*

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390 (Code 38), giving full name, rank, corps, old and new addresses, and zip code.

The issuance of this publication approved in accordance with NAVEXOS P–35.

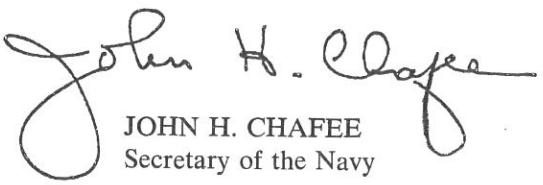
## TO THE OFFICERS OF THE MEDICAL SERVICE CORPS

On the 22nd Anniversary of the establishment of the Navy Medical Service Corps, it is with pleasure that I extend greetings and congratulations to each of you.

The men and women who comprise your Corps have a well deserved reputation for their abilities, devotion to duty, and spirit of service which have greatly contributed to the successful accomplishment of our mission. Since the prevention of disease and injury and the care of the sick merit the finest capabilities, you should all be proud that your many and varied skills play such a vital part in these functions.

I want you to know that I have complete confidence in your ability and willingness to face the future and discharge your responsibilities in full measure.

I extend my best personal regards and wish you a HAPPY BIRTHDAY!



JOHN H. CHAFEE
Secretary of the Navy

It is with pride and pleasure that I extend to you my most hearty congratulations on the 22nd Anniversary of the establishment of the Medical Service Corps and I assure you that all members of the Navy Medical Department join me in these felicitations.

Your enviable record of accomplishments, both individually and collectively, fully justifies the pride that is so evident among all officers of your Corps. I would like to express my sincere thanks to you for the support you are giving me and I want you to know that I have every confidence that you will continue to discharge your responsibilities and accept new challenges with the same determination you have so ably demonstrated during the past 22 years.

To each and every one of you, wherever you may be serving, I send my warmest regards and wish you a HAPPY BIRTHDAY!

G. M. DAVIS
Vice Admiral, MC, USN
Surgeon General

On this occasion of the Twenty-Second Anniversary of the establishment of the Navy Medical Service Corps, it is with sincere pleasure that I extend to all of you my hearty congratulations and best wishes.

Your Corps has notably distinguished itself through the past years by the dedication, pride of service, and performance of duties so brilliantly exemplified by its officers. The support that you have rendered to the Medical Department has been marked by a strong sense of purpose and a high degree of professionalism. I am especially grateful for the unselfish contributions of time, talents, and energy given by those officers who have served with the Dental Corps. The success of our health-care team has truly been enhanced by your efforts.

Best wishes from the officers of the Dental Corps for a HAPPY BIRTHDAY!

E. C. RAFFETTO
Rear Admiral, DC, USN
Assistant Chief of the Bureau of
Medicine and Surgery (Dentistry)
and Chief, Dental Division

I am both proud and pleased to have this opportunity to extend my personal greetings to all of you on this Twenty-Second Anniversary of the establishment of the Navy Medical Service Corps.

This anniversary is an appropriate occasion to reflect back on the past accomplishments of our Corps with pride and gratification. It is also a proper time to look forward and resolve that we can and will make even greater contributions and assume additional responsibilities in fulfilling our future role within the Navy Medical Department. I have every confidence that we will do so with the same zeal and determination the members of our Corps have so consistently displayed during the past 22 years.

To each and every one of you a most HAPPY BIRTHDAY!

E. L. VAN LANDINGHAM, JR.
CAPT, MSC, USN
Chief, Medical Service Corps

# MEDICAL ARTICLES

## TIME AND ITS EFFECTS ON CASUALTIES IN WORLD WAR II AND VIETNAM

*LCDR Lee P. Haacker, MC USNR, Great Lakes, Ill., Arch Surg 98(1):39–40, January 1969.*

The expression, "time has both the quality and quantity," is well appreciated by the man in combat today. He is well aware that if he is wounded, his survival depends upon the "quantity" of time allowed him by his particular injury, and he also knows that the "quality" of the time allowed him in the form of medical care is equally critical.

Each soldier and marine today is also aware that vast changes have taken place in casualty care since World War II, and that his chance of survival is much greater than his father's or uncle's was in World War II. This knowledge has been a tremendous morale factor among the men in Vietnam.

Assuming an open fracture, the casualty of World War II was treated in the field by the corpsman or medic, and carried to Battalion Aid Station (BAS) by litter, ambulance, or jeep. Here, first aid only could be offered, and plasma or blood was usually not available. This evacuation, the first echelon of treatment, usually took from 1 to 12 hours, and the patient frequently stayed at this facility 4 to 24 hours before further evacuation could be effected. He was then evacuated, usually by ambulance, over rough roads several miles to the clearing company where plasma and blood were available, and the first definitive surgery could be performed. His arrival was usually from 8 to 36 hours from the point of injury, and he frequently stayed at this facility from one to ten days before further evacuation. With an open fracture, only soft tissue debridement was performed, and splinting suitable for transportation applied. Further evacuation to a rearward hospital, perhaps in France, frequently found him five to ten days from the time of injury. Here, the first definitive surgery such as treatment of the fracture fragments, further debridement, and the application of skeletal traction was performed. After approximately 21 to 120 days, the patient might have been evacuated to a permanent hospital in Great Britain by land or possibly by air on a C-47. If further evacuation to the United States was contemplated, it was by hospital ship, often four to six months from the time of injury.

Today in Vietnam, the patient is treated in the field by the same corpsman or medic with the same techniques of first aid. The patient is usually air-evacuated by helicopter to a collecting and clearing company with field hospital facilities. The BAS is completely bypassed and the entire trip is frequently within 10 to 20 minutes. Definitive surgery including treatment of the fracture fragments, chest, or abdominal wounds is performed here, and any immobilization for transportation applied as is necessary. When the patient is transportable, usually in 24 to 48 hours, he is air-evacuated by jet plane in a three to four-hour flight to Clark Air Force Base in the Philippines. Here the patient remains with the casualty staging unit, independent of the hospital, where he is reexamined. If his status necessitates further treatment, he is admitted to the hospital. Otherwise, within another 24 to 48 hours, he is on his way, by jet plane, to an armed forces hospital within the continental United States. He is in flight approximately 15 hours to Andrews Air Force Base in Maryland, where he is again reexamined prior to being transported to his final destination. Casualties not infrequently arrive at the Naval Hospital, Great Lakes, Ill., within 72 to 96 hours from the time of injury.

This conservation and better utilization of time, when combined with the medical advancement in the intervening 25 years have allowed us to save 98 percent of the casualties in Vietnam, compared to 94 percent to 96 percent of those of World War II. Add to this the casualties reaching treatment facilities today who would not have survived long enough in World War II, and the apparent increase of 3 percent assumes greater significance. The mortality in Vietnam is lower than in any other major conflict, in that only 2.4 percent reaching medical facilities have died. The comparative figure for World War II is 4.5 percent, and 8.5 percent in World War I. Mortality of those surviving the first 24 hours is considerably less than this.

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From the Naval Hospital, Great Lakes, Ill.
Reprint requests to 4400 Stamp Rd, Marlow Heights, Md. 20031 (Dr. Haacker).

There are three significant factors involved in this renaissance of casualty treatment and handling. The first comprises medical advancements including improved medical techniques and resuscitation equipment, and the second, the availability of vast quantities of blood, both whole and frozen. The latter can be stored practically indefinitely and allows larger quantities of blood to be available for longer times. Antibiotics, often taken for granted, merit inclusion in this factor. Better training in vascular surgery and the availability of better equipment has resulted in the saving of many previously doomed limbs and patients. Some estimates indicate that we are saving 75 percent to 80 percent of limbs that would have been lost in World War II. Transfusions of 40 to 50 units of whole blood are not uncommonly noted in hospital records of air-evacuated patients, and one case of a 93-unit replacement with survival has been recorded, as noted by RADM J. W. Albrittain, MC, USN (oral communication, 1967).

The other two factors involve transportation. They are the helicopter and the C-141 *Starlifter* transport jet, operated by the Military Airlift Command.

The helicopter, first introduced in the Korean Conflict, has reached maturity in Vietnam. It offers speed, versatility, and adaptability. It can be on the scene in minutes, often landing in otherwise unaccessible areas, and air evacuate a seriously injured patient to a field hospital, frequently in less than 10 to 15 minutes. Thanks to it, the longest ambulance ride may be 10 meters, compared to 10 miles in World War II. In the first four months of 1967, one group of medical evacuation helicopters, called "Dust-Off" helicopters, because of the rapidity of their arrival and departure, lifted 12,000 wounded men to medical care, as noted by RADM J. W. Albrittain, MC, USN (oral communication, 1967).

The last factor is, if nothing else, a formidable one. The huge Lockheed C-141 *Starlifter* has been used since the summer of 1965 in returning wounded to the continental United States. Its capacity is 80 litters, approximately twice that of the C-135 or military version of the Boeing 707, and seven to eight times the capacity of the World War II C-47. With its cruising speed of 485 mph, the west coast of the United States can be reached from the Philippine Islands within 13 hours, with only one refueling stop. This transport may also be converted to carry 124 ambulatory patients or a combination of both. It can be ready for litter carrying within 25 minutes, complete with oxygen outlets and facilities for suction,

*Casualty Flow in World War II as Compared to Vietnam*

| World War II Field | | Vietnam Field | |
|---|---|---|---|
| Time Period | Point of Treatment | Time Period | Point of Treatment |
| 0-12 hr (4-24 hr) | BAS | 15-45 min (24-48 hr) | IPH† Ship Station CCCO Hospital |
| 8-36 hr (1-10 days) | CCCO* Field Hospital | 36-72 hr (24-48 hr) | Clark AFB |
| 5-10 days (21-120 days) | Evacuation Hospital (France) | — | |
| 21-120 days (7-28 days) | Rear Hospital (Great Britain) | — | |
| 4-6 months | CONUS | 72-96 hr | CONUS (Andrews AFB) |

* A collecting and clearing company or the Navy equivalent of a field hospital.

† Landing platform helicopter, a small carrier designed for helicoptic use. It may be equipped with surgical facilities including operating room for handling casualties directly from the field by helicopter.

and such innovations as a lightweight, air-borne respiratory, specifically designed for air evacuation. The pressurized cabin allows the safe transportation of seriously wounded casualties far above the surface air turbulence. These planes are staffed with a trained paramedical crew capable of handling practically any transportable patient. If the indication is present, a medical officer frequently accompanies the patient. Since 1954, of the nearly 66,000 patients handled in this manner, only seven have died in flight.

These factors have caused a revolution in medical casualty handling, which becomes apparent when one makes some simple comparisons (Table). It is now possible to take a wounded man from the field to a hospital facility, operate, performing definitive and life-saving surgery, transport the patient to a Naval Hospital within the continental United States, and close his wounds in the time it formerly took to move a patient from France to a British hospital. It is now possible to travel from Clark Air Force Base in the Philippine Islands to Andrews Air Force Base on the east coast of the United States in the same time that it took a World War II casualty to be removed from the field to a BAS.

It is now possible to have an injured patient in a well-equipped operating room with up-to-date resuscitation equipment within 20 minutes from the time of injury. It is now also possible to remove a patient 8,000 miles from his point of injury to a

definitive treatment point in the United States within 72 hours, having paused along the way for definitive surgery. We now routinely fly air evacuees at a rate of speed faster than our fastest World War II fighter pilot flew. Lastly, we are seeing patients arrive, nonchalantly discussing injuries that would not have allowed them to survive long enough to reach the first echelon of treatment in World War II.

(The references may be seen in the original article.)

## THE USE AND ABUSE OF LABORATORY TESTS

*Henry P. Russe, MD FACP,* Med Clin N Amer 53(1):223–231, January 1969.*

If humans, to paraphrase Osler, are distinguished from other primates by their need to take drugs, then physicians must be distinguished from other men by their need to order laboratory tests.

The papers in this symposium indicate that an increasing array of diagnostic studies assists the clinician in the practice of medicine. One need only look at the title pages of current general medical journals to be impressed with the importance of newer laboratory procedures in the recognition and treatment of common diseases; and for the outsider, the complexity of advanced techniques discussed in the specialty journals may be overwhelming.

The rate of growth has been most rapid in the area of biochemical determinations, but other types of quantitative and qualitative measurements of body activity have also flourished. Many new tests represent applications of current research techniques to clinical problems and thus speak for a deepening knowledge of basic mechanisms of disease.

Appropriately used, laboratory tests strengthen the physician's diagnostic precision and improve his management of the disordered physiology of disease. However, the proliferation of tests has also increased the opportunity for their excessive, unnecessary, and unwise misuse.

### Use of Laboratory Tests

Our basic medical education stresses the primacy of a thorough history and physical examination in reaching the proper conclusion, with laboratory studies adding only certainty to the diagnosis or defining the magnitude of the disorder. How different from this older attitude is the present trend to rely on the "routine" laboratory determinations to suggest the nature of an illness! How wonderful the future may be when computers will not only secure and interpret a history from the patient but collate historical data with multiphasic screening of all systems to arrive at a statistically valid rank order of probable diagnoses and a programmed therapeutic regimen. Present models of computer applications make the diagnostic machine more than a science fiction illusion, but until some future time, the physician must still select, understand, interpret, rely upon, and sensibly employ laboratory studies of great diversity in the delivery of health care for the greatest benefit of his patients.

There are certain diseases in which little can be added to an impression based on a history of the illness. The classic migraine headache, for example, may be the only clue to the diagnosis, while physical examination as well as laboratory studies can all be normal. At the other extreme, a vague complaint of fatigue may bring a patient to the attention of a physician, who notes an anemia. When this is characterized as Coombs-positive and hemolytic in nature, an immunoelectrophoresis is done which shows an abnormal globulin—leading ultimately to the diagnosis of a malignant lymphoma that would not have been discovered without the assistance of laboratory tests.

Proper analysis of the clinical situation must be based on all sources of information, including history, physical examination, and appropriate laboratory studies. Total reliance on laboratory studies may reflect inexperience, omission of laboratory evaluation may indicate lack of medical skill, and either extreme could be detrimental to the patient.

### Routine Laboratory Tests

Since laboratory evaluation has become accepted as a normal extension of the history and physical

* Chief of Medicine, Columbus-Cuneo Medical Center, Chicago; Associate Clinical Professor of Medicine, Loyola University Stritch School of Medicine, Hines, Illinois.

examination, usually some sort of blood counting and an examination of the urine for protein and reduction are standard as part of the "complete examination." The question of what constitutes an acceptable amount of laboratory testing is one which remains largely unsettled. The Joint Commission on Hospital Accreditation has suggested for many years that all patients admitted to a hospital must have a history, physical examination, and certain minimal laboratory tests. By conventional interpretation of this edict, most hospitals have, until recently, considered that a more or less complete blood count (hemoglobin, white blood cells, and differential), a urinalysis (specific gravity, pH, tests for reducing substance and protein, and a microscopic examination of the sediment), a chest x-ray, serologic test for syphilis, and a cervical smear for cytology on mature women are the usual diagnostic laboratory procedures routinely to be done on all admissions. To these basic studies many physicians feel that certain screening tests should be added, including an electrocardiogram and selected blood chemistries. Obviously, the use of increasing numbers of screening tests might detect an abnormality not suggested by either history or physical examination, but the return in terms of real numbers on such an evaluation may be slight.

Diversity of opinion regarding the desirability and utility of routine testing has recently been presented editorially. Since laboratory tests are not only a potential source of discomfort to the patient and a certain source of expense to him, unnecessary tests should be kept to a minimum.

## Medical Costs

The cost of medical care has been a subject of great concern to economists, governmental agencies, and certainly to the consumer. One of the significant costs of health care is directly related to the number and kind of laboratory tests done on the patient. Several third-party health insurance carriers will not cover expenses incurred for the purpose of diagnostic studies unrelated to treatment of an injury or illness. Their attitude on this point is certainly understandable. Assuming that only a small part of the $37 billion spent in 1965 for health services in the affluent new health-care economy described by Darley went to pay for laboratory tests, and if, as he predicts, we may expect to see an increase beyond this astronomical figure of upwards of $10 billion every 2 or 3 years in the future, it is easily seen that some limitation of unproductive laboratory test costs is mandatory for survival of the present system of health insurance carriers.

The physician is thus placed in a situation where he must consider not only the needs of the patient for completeness of laboratory testing, but also the cost of extensive screening. The difficulty of defining and measuring the cost, especially the cost of neglect, as emphasized by Darley, is great. Despite this huge amount of money spent on health, there has been no demonstrable increase in longevity for men in the United States since 1954 and only a small increase for women. This apparent plateau persists despite an emphasis on quantity in health services paralleled by an increase in the number and kinds of diagnostic studies available to the clinician which the sophisticated patient may request or actually require.

With the development of automated techniques, it is now possible to increase the productivity of a laboratory and reduce the unit cost of specific tests if groups of tests are run on the same sample. This has the effect of reducing the cost to the patient for a single item in a group although the charge for the entire study may raise his total laboratory bill. In another section of this symposium, multiphasic screening tests are discussed in detail (p. 175), but here it may be mentioned that the smaller hospital particularly may benefit from the increased quality that automated procedures can provide, and the length of patient stay may be cut by multiple determinations on a single sample, rather than daily sample testing.

Although economic factors are very significant in considering the use of routine or screening laboratory tests, one of the most important reasons for such testing is to facilitate the early recognition of unsuspected disease or the discovery of a premorbid state of health. Examples of the uses of such testing are: routine chest microfilming to detect tuberculosis or other chest diseases, which discovers several thousand new cases of active tuberculosis annually in addition to those suspected on the basis of mass skin test surveys; mass urine and blood sugar screening for diabetes, with numerous asymptomatic cases discovered annually and treated; screening for the presence of hyperaldosteronism in the hypertensive patient by means of sodium loading and observation of serum potassium levels. The patient with primary aldosteronism will develop a serum potassium below 3.5 mEq. per liter after 4 days with a sodium intake in excess of 200 mEq. daily, whereas the normal hypertensive patient will maintain a stable serum potassium.

These and many other types of screening tests are now being employed in regional health surveys, in teaching centers and in community hospitals as well as in individual medical practices. The reliability of such testing in distinguishing diseased from healthy persons is dependent on its sensitivity and specificity. This point will be discussed subsequently.

Because of the utilization of automated equipment capable of providing rapid surveys of a panel of diagnostic tests done on admission to the hospital, the entire attitude and approach to laboratory medicine has been changed. At Barnes Hospital, St. Louis, during a period when 35,000 chemical profiles were done with automated equipment and 511 patients' records were examined and compared with test results, in 61 cases the laboratory data suggested clues to unsuspected disease. This approaches a rate of 12 percent occult disease in a hospital population, a figure quite similar to that reported by Levine and Crosbie as the diagnostic yield in a routine abdominal x-ray examination, where 26 of 242 patients had unsuspected pathologic findings.

Aside from the obvious increase in diagnostic accuracy that screening tests give to the physician, according to the figures cited above, the patient probably derives a real benefit from the knowledge that his physician's diagnostic skills are expanded by such testing. This may be especially true if the patient realizes that either the history or examination has been abbreviated for any reason.

Amidst a welter of enthusiasm for the use of routine or screening laboratory tests, an occasional voice of protest speaks out. Dr. Walter Alvarez pleads for restraint and the sensible use of the laboratory test, while marveling at the fact that so many patients have no interest in a clinician's opinion of their problem, but would rather have tests—the more, the better, and often a repetition of recent studies that were normal in another laboratory.

He further notes that today's doctor may have to order needless tests to avoid the possibility of subsequent suit by a patient claiming neglect. This concern is most common in trauma cases and primarily involves radiologic evaluations, but it is not too difficult to envision the day when negligence might be upheld if a routine test was not done that might have detected an early, more easily treatable form of a subsequently manifest disease.

## Factors Influencing Interpretation of Tests

The variations of human biologic reactivity in health and disease are enormous and may lead to great confusion in the interpretation of laboratory data unless the physician is aware of the factors which affect test results. Some of these are: reliability of the method or the analytical equipment with which the test is done; technical skill of laboratory personnel; effectiveness of laboratory quality control; standards of normal values for the test in the performing laboratory; extraneous factors affecting results; interdependence of variables related to the patient and his disease; sensitivity and specificity of the test; and cooperation of the patient, to name a few of the more important ones.

Reliability of method and equipment are properly in the realm of the clinical pathologist and ordinarily do not concern the physician caring for the patient unless he is performing some of the determinations himself, but they obviously are important sources of potential error. The same comments apply to the technical skills of the laboratory workers and the results they produce. Knowing that the laboratory uses reliable methods and people is reassuring when an abnormal laboratory value means the difference in choice of treatment or a change in therapy.

The effectiveness of laboratory quality control is the subject of rather spirited accusation and defense in the literature, with a constant effort by the College of American Pathologists to bring laboratories up to acceptable standards through a program of periodic surveys. Particular attention has recently been given to the small community hospitals. The accuracy and reproducibility of determinations done on known samples prepared for analysis of such common items as blood glucose, blood urea nitrogen, serum proteins, and hemoglobin, have been rated as satisfactory, acceptable, and unacceptable according to performance within predetermined statistical limits. This kind of survey has real importance when one considers that over three fourths (4430 of 5610) of the acute disease, nongovernment hospitals in the United States have 100 beds or less. The interesting finding, reported in a 1966 survey of the Standards Committee of the College of American Pathologists, was that the great majority (85 to 90 percent) of small hospital laboratories performed acceptable or satisfactory work on most prepared samples and that the unacceptable results could be related in part to the method used for the determination in question.

This report is reassuring, but in sharp disagreement with one by Kaufmann and Vanderlinde that confirms earlier studies which suggest that there are serious deficiencies in the performance of laboratory tests in hospital and independent laboratories.

In a survey in New York State, Kaufmann and his coworker found that both hospitals and independent laboratories which performed less than 1,000 tests annually produced unsatisfactory results. Their figure of 60 percent unsatisfactory results for hospital laboratories is staggering, and the 41 percent cited as unsatisfactory for the independent laboratory is equally disturbing. In their study the small hospitals did particularly poorly, due no doubt to the limited number of annual determinations, while laboratories with more than 100,000 annual tests were all above the 75 percent acceptable figure for accuracy.

The clinician's interpretation of tests is influenced by the set of normal values the particular laboratory has generated for that determination. A common standard for comparing results of clinical measurements is the range of values for a series of determinations on normal people. Here the nondiseased person is considered to be normal, and a statistical grouping of many normal values thus should provide a set of values for comparison with the patient. If his test result falls more than an arbitrarily defined distance outside the normal range, it is abnormal and presumably indicative of disease. One obvious disadvantage of this type of reasoning is that it does not allow for the unusual person whose test value may fall outside the prescribed ideal normal and yet not truly indicate disease. A further problem with the concept of the normal range lies in the origin of the "normal" values. Wintrobe cites the remarkable example of the normal range for red blood cell count which is based upon determinations made on four subjects more than 100 years ago! The concept of normality based upon determinations made on laboratory workers, medical students, nurses, and blood donors is further biased by the selection of the "normal" persons. This kind of sampling is not random and bears no true relationship to the population of diseased patients later to be tested and compared with the normal range. Despite these shortcomings the normal range has utility if the physician is aware of its limitations. Benson's brief review of the concept of the normal state helps clarify some of these points.

Extraneous factors may affect laboratory test results in obvious or subtle ways and add to the difficulty of interpretation. The consequences of an incomplete collection of urine when a creatinine clearance test is done are easily predicted, but unless the physician knows that the collection was incomplete, the result of the test might be taken at face value. A forceful ejection of a blood sample into the collection container will hemolyze red blood cells and spuriously elevate serum potassium values, as we all know, but this extraneous influence on test results could have profound consequences in a patient with renal failure in whom the serum potassium was being monitored and emergency measures to lower potassium were instituted and wasted for later use when the need might be real.

Drugs may be an unexpected factor in the interpretation of laboratory tests due to their effect of modifying blood levels of normal constituents. The action of salicylates and thiazides on uric acid levels is well known, but if the patient neglects to inform the physician he is taking these medications, or if he does not consider aspirin a drug and neglects to mention it for this reason, an improper diagnosis of gout could be made and unnecessary treatment initiated. Many other examples of the effect of drugs on laboratory tests could be mentioned, but this topic is discussed at length elsewhere (p. 211).

One of the most difficult problems in the interpretation of laboratory tests is that of interdependence of variables. Frequently the physician may not be aware of this dependence, or at least not certain of its importance. In this vague area the effects of the disease process on uninvolved organ systems may play a role in alteration of normal values leading to confusion.

The specificity and sensitivity of a laboratory test are of importance in distinguishing diseased from nondiseased patients. Sensitivity is defined as the ability of a test to yield a positive finding when the person studied truly has the disease, whereas specificity may be defined as the ability of the test to give a negative finding when the person tested is free of the disease in question. Both of these parameters must be considered by the clinician in his interpretation of laboratory results as well as the possibility of false positives and false negatives.

Not the least of the factors influencing the results of laboratory studies are the cooperation, attitude, and emotional state of the patient. If the examination requires a timed collection, was it accurate? In a performance type of examination, was the patient motivated to do his best? If physiologic measurements are a part of the test, what was the state of the patient? Was he relaxed or tense? If the determination of a blood chemistry required the fasting state, had the patient eaten? All these seem quite obvious, but may cause unnecessary repetition if the patient is not made aware of the need for his understanding and cooperation.

## Abuse of the Laboratory Test

Implicit in the conditions enumerated above for the sensible and productive use of laboratory examinations of the patient as an aid to diagnosis and treatment are several practical and economic considerations to avoid abuse of the laboratory. Many additional abuses are detailed by Zieve and include both deliberate and unintentional misuse of the laboratory related to lack of information on the part of the physician and probably in large measure to use habits as well.

According to Zieve, most clinicians interpret the tests they employ without knowing how the tests are performed or the assumptions used in the calculation of results. As an example he chooses the bromsulphalein test of liver function to point out the relationship between the dose of drug given and the size of the patient. The normal values for this particular test are based on standard factors related to the patient's size and blood volume, and the excretory rate of a presumably inert substance. Allowance must be made for the patient's size to use this test reliably, but this is seldom considered in the evaluation of results, since the same amount of dye is routinely given to each patient. Zieve mentions that interrelationships between obstructive jaundice and tests of thyroid function often go unrecognized. Spuriously high values for protein bound iodine as a consequence of the normal excretion of thyroxine by the liver cell can occur in biliary tract obstruction, and if the physician is unaware of this relationship, further unnecessary tests of thyroid function are usually requested, increasing the laboratory work load and yielding no useful information. These types of laboratory abuse are unintentional, but still costly to the patient. Education is the answer to problems like these. Here the clinical pathologist in the role of a consultant colleague can be helpful, both in terms of selection and interpretation of tests.

One of the most unfortunate abuses of the laboratory is related to gamesmanship on the part of the doctor ordering the tests. Because of a desire to impress the attending physician with his erudition, the consultant may order unusual or little-known studies on the patient. Such studies are frequently of limited value in establishing a diagnosis or modifying therapy, but they clearly put the consultant one up on his peers. If the laboratory is able to comply with the consultant's suggestion and perform an obscure test, very likely the result will be of questionable validity since no one has done that procedure before. This spurious abnormal value can then be pounced upon by the gamesman, leading to a spiraling of more tests ad absurdam. Fortunately this type of one-up-manship is rare in most medical communities.

Another abuse of the laboratory is the unreasonable habit many physicians have of ordering a serial repetition of tests as a routine and continuing the search after one or more of the initial values have been reported as positive. In the age of the overkill, perhaps this sort of rationale is to be expected, but it does nothing for anyone—patient, doctor, or technician. A variant of this sort of reasoning lies behind the repetition of tests when the result does not agree with the clinician's preconceived and sometimes erroneous ideas about the result. Certainly a healthy skepticism on the part of the doctor is admirable and often correct, but stubborn persistence is another matter.

Often tests are requested unnecessarily because the clinician vaguely remembers an association between a disease process and a given test or a relationship between tests which measure the same function. In this instance a battery of tests might be requested when only one or two would suffice.

Frequently, when a battery of tests such as a liver profile or a hemogram is done, one value may be reported as abnormal. This observation could have significance and is therefore to be followed—but not with a repetition of the whole battery when repetition of the one test is all that is required. Serial testing after an abnormal value is noted frequently gives information about the response to therapy or progress of the disease, but tests are repeated much more often than the patient's change in course demands for careful surveillance of the problem. Regular repetition of tests often continues beyond the point at which the condition has been resolved or stabilized.

Abuse of laboratory tests may be a sin of omission as well as commission. It is now possible, by means of appropriate studies, some simple, some complex, to diagnose an increasing number of diseases that are amenable to treatment and to seek a cure. Surely a significant abuse would be the omission of the studies to confirm a diagnosis in these cases because of misplaced thoughts of thrift or other considerations equally unimportant in terms of the cost of the ultimate results.

## Summary and Conclusions

Great advances in the techniques of measurement

of biologic phenomena have given rise to an increasing number of laboratory tests which extend the clinician's diagnostic skill and guide his therapeutic efforts. Unfortunately, this technically increased capability is accompained by increases of cost and complexity of laboratory tests. The physician must be sufficiently well informed about laboratory procedures to select those which are most likely to give him an accurate evaluation of the problem he seeks to solve and which can be most reliably and inexpensively performed by his laboratory facility. Abuses of the laboratory are often based on lack of understanding of the person ordering the tests.

(The references may be seen in the original article.)

# OCULAR COMPLICATIONS OF DRUGS

## GLAUCOMA

*W. Morton Grant, MD, JAMA 207(11):2089–2091, March 17, 1969.*

Glaucoma, whether spontaneous or drug-induced, is caused in nearly all instances by abnormal resistance to outflow of aqueous humor to the veins on the outer surface of the eye. Three types of glaucoma can affect adults: angle-closure glaucoma, open-angle glaucoma, and the secondary glaucomas that result from preexisting ocular diseases. The adverse effects on intraocular pressure produced by systemic drugs principally involve the first two types of glaucoma.

An acute attack of angle-closure glaucoma, which may be precipitated by drugs that dilate the pupil, is caused by the periphery of the iris bulging forward to obstruct the trabecular meshwork and, thus, prevent the aqueous from reaching the outflow channels. In open-angle glaucoma, which may be aggravated by anticholinergic and corticosteroid drugs, excessive resistance to outflow is caused by changes within the outflow channels themselves, mainly within the trabecular meshwork, independent of the size of the pupil.

The intraocular pressure usually goes higher in angle-closure glaucoma than in open-angle glaucoma. Angle-closure glaucoma tends to develop acutely, with blurring of vision, halos, and often pain, whereas open-angle glaucoma tends to be chronic, and commonly occurs without warning symptoms. Acute angle-closure glaucoma is an emergency condition that can cause blindness if not quickly recognized and treated. It nearly always requires intensive medical treatment followed promptly by surgery. Chronic open-angle glaucoma, on the contrary, usually can be controlled medically for long periods, and visual losses occur relatively slowly if it is not controlled.

A tonometer is a valuable tool for detecting the elevation of intraocular pressure characteristic of any type of glaucoma. The Schiotz instrument is preferable for routine medical use. With it, measurements are made with the patient recumbent and looking at the ceiling with both eyes open. After the cornea is anesthetized (I use 1 drop of a 0.5 percent solution of proparacaine hydrochloride in each eye, repeated once in 10 or 15 seconds), the patient's eyelids are held gently apart so they do not touch the instrument, which is held vertically overhead and rested on the cornea. In about four seconds, a reading is made of the position of the indicator on the scale. If the reading is not reasonably steady, the tonometer is lifted, reapplied, and read again. When the tonometer is used alone without supplementary weights, a scale reading of 4 or less indicates the necessity of further investigation into the possibility of glaucoma. After completing these readings, a drop of a suitable antibacterial ophthalmic solution may be applied to the eyes.

The diagnosis of open-angle glaucoma is based primarily on finding chronically elevated intraocular pressure, which may or may not be accompanied by glaucomatous cupping of the optic nerve head and other characteristic abnormalities of the visual fields. However, tonometry cannot be depended on as a means of foretelling whether a person is predisposed to development of glaucoma of the angle-closure

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and Massachusetts Eye and Ear Infirmary, Boston.
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Reprint requests to Secretary, Council on Drugs, American Medical Associatian, 535 N Dearborn St, Chicago 60610.

type because, in this type, the intraocular pressure may be entirely normal prior to an attack. Fortunately, the combination of farsightedness, abnormal convexity of the iris, and a characteristic narrowness of the space between iris and cornea is helpful in predicting that a patient may be subject to the development of angle-closure glaucoma.

The presence of an anatomical predisposition to angle-closure glaucoma is best determined by examining the angle of the anterior chamber with an ophthalmic biomicroscope and gonioscope. However, when this is not feasible, a useful estimate of whether the space between the iris and cornea is abnormally narrow can be made by holding a small prefocused flashlight close to the eye, concentrating the light on the cornea and iris from the temporal side. In persons who are predisposed to the development of angle-closure glaucoma, the iris appears bulged forward, close to the posterior surface of the cornea. In average, normal eyes and in nearsighted eyes that present little or no risk of angle-closure, the iris appears almost flat and the distance between the iris and the posterior surface of the cornea is distinctly greater than it appears in angle-closure glaucoma. In patients with open-angle glaucoma, the space usually appears normal.

## Anticholinergic Drugs

Patients with normal eyes, not predisposed to either angle-closure or open-angle glaucoma, apparently can receive topically administered drugs with anticholinergic effects, without causing any significant elevation of intraocular pressure, regardless of the effect on the pupil or on accommodation. However, in patients more than 30 years of age who have abnormally shallow anterior chambers and narrow angles, there is risk of precipitating angle-closure glaucoma if the anticholinergic drug is one that causes the pupil to dilate (eg, atropine, amprotropine, cyclopentolate, homatropine, scopolamine). Also, if the drug causes paralysis of accommodation, it can aggravate open-angle glaucoma by increasing the resistance to aqueous outflow, which tends to raise intraocular pressure and sometimes raises it to the point of damaging vision if maintained for a long period.

In a racially heterogenous North American population not screened with regard to glaucoma, topical administration of an anticholinergic agent may be expected to induce acute angle-closure glaucoma in approximately 1 in 4,000 persons more than 30 years of age. It may also be expected to aggravate preexisting or latent open-angle glaucoma in approximately 1 in 100 persons more than 40 years of age.

Anticholinergic drugs may produce the same ocular effects when they are administered systemically, but the quantity of drug reaching the eye and, therefore, the intensity of action often are much less. Occasionally, when atropine is given systematically as a preoperative measure, enough of it reaches the eye to cause considerable dilation of the pupil and, in predisposed persons, causes the precipitation of acute angle-closure glaucoma.

In patients known to be predisposed to closure of the angle, drugs that are administered orally, or that have weaker anticholinergic properties (eg, antihistaminic, antiparkinsonism, antipsychotic, gastrointestinal spasmolytic drugs) present a risk that is proportional to their effect on the pupil. Tests indicate that anticholinergic drugs with little or no effect on the pupil (eg, anisotropine methylbromide, dicyclomine, methixene hydrochloride) also have little or no tendency to induce glaucoma. Amitriptyline hydrochloride, which may moderately dilate the pupil, was studied in Austrialia and estimated to be associated with acute angle-closure glaucoma in approximately 1 in 1,000 users not preselected by eye type. There is insufficient evidence to determine whether amitriptyline actually caused glaucoma in these rare instances. When angle-closure glaucoma does occur in a patient being given a drug that dilates the pupils, it may be difficult to ascertain the role of the drug with certainty, since spontaneous occurrence of this type of glaucoma is common in predisposed eyes.

The use of systemic anticholinergic drugs presents less of a problem in patients with chronic open-angle glaucoma than in patients threatened with angle-closure glaucoma since, in the chronic disease, one can administer the drug and determine by tonometry whether the intraocular pressure is appreciably affected without risking the precipitation of an acute emergency. The relative degrees of paralysis of accommodation observed seem to indicate that most systemically administered drugs have less tendency to produce anticholinergic effects in the eye and thus increase intraocular pressure than do the topical ophthalmic preparations of atropine, homatropine, and cyclopentolate. In patients already under treatment for open-angle glaucoma, it is probable that in most instances, the potential adverse effects of systemically administered anticholinergic drugs would be completely counteracted by the drugs being used for the treatment of the glaucoma. Close examina-

tion and regular tonometric measurement are needed to determine whether the antiglaucoma drug regimen is adequate to maintain control of the intraocular pressure in the presence of the systemic anticholinergic drug.

### Adrenergic Drugs

Some orally administered drugs that have adrenergic properties, such as vasoconstrictors, central nervous system stimulants, appetite depressants, and bronchodilators (eg, ephedrine, amphetamine, dextroamphetamine) can also dilate the pupils, although seldom to any striking extent. They do not appreciably affect accommodation. They have no proven adverse influence on intraocular pressure in either normal eyes or in those with open-angle glaucoma, but it has not been conclusively ruled out. Patients beyond middle age who have abnormally shallow anterior chambers and abnormally narrow angles are anatomically predisposed to closure of the angle if the pupils become sufficiently dilated. This can occur spontaneously as well as being induced by topically applied adrenergic or anticholinergic mydriatic agents. The actual incidence of angle-closure glaucoma induced by systemically administered adrenergic drugs is unknown, but it probably is less than that from anticholinergic agents. Hallucinogenic agents that dilate the pupils could presumably also precipitate angle-closure glaucoma in the same type of patient.

### Vasodilators

Vasodilator drugs were long supposed to be hazardous for use in patients with glaucoma, but this probably was a misapprehension based on theories of glaucoma that have undergone significant revision. There is no convincing proof that vasodilator drugs administered systemically induce or significantly aggravate glaucoma, despite the fact that subconjunctival injection of strong vasodilators (eg, bamethan sulfate, isoxsuprine hydrochloride, tolazoline) can induce a transient rise of intraocular pressure, especially in eyes with chronic open-angle glaucoma. In patients with abnormally narrow angles, attempts have been made to induce angle-closure glaucoma by administration of nitrate and nitrite vasodilators, but so far there is no evidence that glaucoma has been produced in this way.

Clinical observations indicate that in both normal and glaucomatous patients it is safe to use orally administered vasodilators, not only of the nitrate and nitrite type, but also tolazoline, dihydralazine, aminophylline, nylidrin hydrochloride (buphenine), nicotinic acid and cyclandelate (J. D. Peczon, MD, unpublished data).

### Systemic Corticosteroids

Repeated topical application of corticosteroids to the eye is well known to raise the intraocular pressure in many persons and frequently to induce severe open-angle glaucoma. However, systemically administered corticosteroids have comparatively little tendency to induce glaucoma. The number of instances of glaucoma reportedly caused this way are few, if one does not consider cases complicated by uveitis or other intraocular inflammation in which the intraocular pressure increases after commencing treatment with corticosteroids given either topically or systemically. Conversely, in patients who already have chronic open-angle glaucoma, there is good evidence that in some cases systemic administration of corticosteroids may make the glaucoma more difficult to control. Therefore, whenever systemic corticosteroids are used in the presence of glaucoma, measurements of intraocular pressure, and observations of the optic nerve heads and visual fields should be done frequently.

### Generic and Trade Names of Drugs

Proparacaine hydrochloride—*Ophthaine.*

Amprotropine phosphate—*Syntropan.*

Cyclopentolate hydrochloride — *Cyclogyl Hydrochloride.*

Methixene hydrochloride—*Trest.*

Dicyclomine hydrochloride—*Bentyl Hydrochloride.*

Amitriptyline hydrochloride—*Elavil Hydrochloride.*

Tolazoline hydrochloride—*Priscoline Hydrochloride.*

Bamethan sulfate—*Vasculat.*

Isoxsuprine hydrochloride—*Vasodilan.*

Nylidrin (buphenine) hydrochloride — *Arlidin Hydrochloride.*

Cyclandelate—*Cyclospasmol.*

(The references may be seen in the original article.)

# COMMENTS ON THE PHARMACOLOGIC WOOF, WARP, AND WEB*

*Irvine H. Page, MD,† New Eng J Med 278(7):364–369, February 15, 1968.*

There is a small segment of medicine called pharmacology. Why should pharmacologists be of any special concern to physicians? Many years ago they chiefly studied mechanisms of the actions of drugs, some useful, most not. Then came a professor of therapeutics who taught medical students what they thought they really wanted to know. But by the nineteen twenties times had changed, and medicine was swept by a wave of therapeutic nihilism. The professor of therapeutics disappeared, and pharmacologists nearly met the same fate. The great wave of chemotherapy saved them, and with the avalanche of new remedies along with the need for governmental control, pharmacologists became greatly in demand and very short in supply . The definition of what constituted a drug, and what were the limits and responsibilities of pharmacology, was so broad that pharmacologists found their activities ranging from becoming vice-presidents of pharmaceutical companies to studying molecular biology. All this causes one to ruminate on the profound changes that have occurred during one's lifetime, many *caused* by pharmacologists. Take the extraordinary shift away from bacterial-induced diseases. Listen to the contents of a doctor's bag less than 100 years ago as described in the 1881 *Canadian Pharmaceutical Journal:* Grindelia robusta (respiratory disease); Yerba santa (bronchitis); Eucalyptus (malaria); Coca (nervous stimulant); Kava-kava (gonorrhea and Sialagogue); Berberis (skin disease); Duboisia (pupil dilator) Chaulmoogra oil (scrofula, rheumatism and leprosy); Nitroglycerin (angina); Tonga neuralgia). In those days a patient could cure half his ills by going to bed and the other half by getting up. Clearly, pharmacologists today are an entirely different breed of cat. And so is the environment in which all of us live and work. I am sure a John Abel, if he reappeared today, would think he was still having a nightmare.

You know the social and legislative discontent and disillusionment that swirls around their heads: therapeutic nightmares, Senator Thalers, Congressional investigations, drug evaluations and experimentation on patients—all under the hot beam of the mass media. No scientist is concerned with more facets of the human enterprise than the pharmacologist. The most recondite chemistry and physiology meld with treatment of human ills, financial support of pharmaceutical manufacturing, deep concern for regulation and evaluation of drugs by the Government, control of environmental factors and cost of medical care.

This indicates a willingness to participate as citizens in the vital decision making, which has all but slipped out of the hands of most medical societies into those of politicians and a few lay advisors. To the great credit of the pharmacological society it has taken this threat seriously and is doing something about it. Its activities, which are being reflected in a most admirable intrasociety journal called, "The Pharmacologist," represent not only the factional aspects of pharmacology but its deep human concerns. This is a sign of social maturity.

We need to take a hardheaded look at the problems now so actively under legislative inquiry. This is an age long on high-sounding phrases, slogans and promises but exceptionally short on accomplishment, as shown by the Atlantic Charter and Watts. More than ever, political man is demonstrating his capacity to act irrationally. The same pattern must not be allowed to dominate the thinking of medicine and science.

Just as the modern corporation and the power to guide it lies in labyrinthian committees, so has science become bafflingly complex. But individuals should not, therefore, lose their identity. When they do, they become compliant. I am sure a committee formulated the plans for the extermination camps in Germany. "I came, I saw and I concurred" may be a handy rule to get ahead in the committee hierarchy, but it is compromise without spine. The meek shall inherit mediocrity. The greatest product of democracy is individual leadership. I am sure it is no news that we are increasingly becoming like a trade union with sharp punishment for deviants from inflexible rules. For those who do not believe this I recommend reading the hearings of the subcommittee on appropriations (United States Government Printing Office). But this increasing rigidity must not be allowed to stifle originality as it almost surely will if it is unopposed.

Now let us look briefly at a few specific problems, in which pharmacologists have been much involved,

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* From the Research Division, Cleveland Clinic Foundation (address reprint requests to Dr. Page at the Cleveland Clinic, 2020 East 93d St., Cleveland, Ohio 44106).

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† Senior consultant, Research Division, Cleveland Clinic Foundation.

the first being membership in societies. For many years a tight rein was kept on the title and on belonging to the official society. By some mystique one became an anointed pharmacologist when one became a member and not before. Is this now an outmoded social operation?

On Being Elected to Membership

A number of societies for many years went through, and still do, the painful, time-consuming and occasionally unjust process of carefully screening candidates for admission. The status and ego of those elected were enhanced. Politics was too often confused with quality. Administrators, scientists and clinicians have become hopelessly confused in many of the most prestigious societies. Yet in retrospect all this selection has come to little. The self-styled "elite of medicine," at least, has disappeared along with the social 400. But the strange part of it is that even though the medical and scientist population has vastly increased, there has been no corresponding increase in available membership. It is the age-old problem that those in need of an inferiority complex never have one.

Being restrictive to maintain standards and tradition had, and still has, its merits, but where do the outer reaches of pharamacology lie? Is a behavioral scientist concerned with the home use of drugs a gilt-edged pharmacologist? What about physiologists? Would you, for example, say that the pharmacology of sexual response qualifies? How could anyone resist this recommendation that appeared some time ago: "Next Spring, Little Brown and Company will publish *Human Sexual Response,* the extraordinarily detailed results of Dr. Masters' eleven years of work with his research associate, Psychologist Virginia E. Johnson."

Physicians face the same problem in paramedical or ancillary health services, or for that matter the great group of influential administrative governmental and academic personnel who have long since defected to the political arena. Should there be special societies for hospital technicians, hospital managers, dietitians, physical therapists, and so forth—all with their time-consuming election mechanisms? Possibly "belonging" is a necessary human trait and we should candidly recognize it.

I urge you to remember that the phenomenal growth of the financial and administrative aspects of medicine has brought a corresponding loss of values. Too often the pleasant but intellectually mediocre person fits comfortably into this increasingly rigid system, which identifies and measures people by the societies to which they are elected. Too many of these have lost the sense of excitement and wonder of discovery; imagination and insight seem to be only for artists. Too often this pedestrian road is quickly rewarded with power, recognition and money. Achievement in science or medicine has been elbowed aside from those who are willing and able to preserve that which has already been. Knowledge and hard work over a lifetime are the inseparable marks of the man we need.

On Experimental Therapeutics

For years the official journal of the Society carried the black words, *Experimental Therapeutics,* in the title, but former editors strongly repressed any efforts to implement either the concept or, I may humbly say, the publication of the results of such research.

Many, many years ago, I sent a paper on the clinical use of amobarbital (Amytal) to Dr. John Abel. He replied in his gentle but concise fashion that I was obviously a very young investigator. Wouldn't I *allow* him to help me put the manuscript into form for publication? Two things: we don't grow editors like that any more, and at that time therapeutics still had a place in pharmacology.

You may remember the early thirties when a wave of therapeutic nihilism struck clinical medicine, largely as a protest against the uncritical polypharmacy. Pharmacologists had decided to clean house and ousted physicians who always "knew of a case" or who refused to abandon such good old remedies as extracts of cornsilk, mistletoe, watermelon and cucumber seeds. Lithia water was also very good for your wife, and I am pleased to see that it is coming back now to treat mania. Remember when lithium was being highly touted as a substitute for table salt in the treatment of hypertension? Lithium ion substituted altogether *too* effectively, and several of my patients slipped into coma!

*Mere* treatment was made to seem hardly worthy of the clinician. If he arrived at a correct diagnosis he was made! You remember the Cabot cases in the *New England Journal of Medicine;* usually, they had already fallen into the hands of the pathologist, so that therapeutics could safely be ignored as, indeed, it was.

By the time I had entered medical school the professor of therapeutics was on his way out. The famous triple-play team of Hatcher to Eggleston to

Gold had replaced Frank Meara at Cornell, and clinical pharmacology had a slightly disreputable image—rather like that of the "rice house" when that therapeutic mayhem called the rice diet was popular. Inexplicably, the greatly respected Council on Pharmacy and Chemistry of the American Medical Association slowly lost its influence. Only with the advent of Senator Kefauver did we realize that we all were in trouble. Close on followed the reorganization of the Food and Drug Administration, set off, I suppose, by thalidomide and Mer-29, although it was already overdue. Sadusk, in his kindly wisdom, started the ball rolling. It didn't roll fast enough, so Goddard took over. Goddard has many of the qualities of his namesake—the Goddard who started rocketry. He is clear-thinking, impetuous, tiresomely tireless, courageous and too often infuriatingly right. With Herbert Ley's help, the somewhat frenetic activist phase is settling down to an effective organization that may get more done at the bedside and less in the White House Rose Garden.

Clearly, experimental therapeutics had to be resurrected. The medical schools were reluctant to re-establish departments of either therapeutics or clinical pharmacology. But there was enough pressure to form new societies, new journals and, bless them, new committees. So now we can all travel and attend meetings with good conscience. The College of Clinical Pharmacology and Chemotherapy and the American Therapeutic Society, the clinical section of your society, have blossomed, and I hope before the bloom is off some grafting will be performed so that the fruit, although bastardized, will still resemble pharmacology. We need statesmanship and concern for the total picture. Diverse societies and journals tend to weaken individual leadership.

Is therapeutics or clinical pharmacology really a specialty? To know the natural history of *all* disease as background for the investigation of proposed treatments is too much. My own experience with hypertension and atherosclerosis is that becoming thoroughly familiar with them takes an unconscionable amount of time. It is not easy to develop rational or even "butterfly-net" treatments. Also, I don't suppose you really believe schizophrenia is unitary—even its name *implies* a split. Although I might be able to plan a therapeutic trial for an anticancer drug, I pity anybody who might have to conduct it. I stopped knowing about cancer when I left Dr. James Ewing at Cornell, took up smoking and came to know Dr. Alton Ochsner.

How, then, can we expect a man to encompass all these disciplines as a clinical pharmacologist? I suspect he will focus his interest on separate categories of disease. I know it is heresy to the older clinicians to suggest extreme forms of specialization. *They* read their own x-rays because a radiologist can't be trusted, nor the laboratory results unless they corroborate their bed-side diagnosis.

Currently, there is too much to know even within the specialties. When I started, cardiology hardly existed. There were a few McKenzies, Lewises, Herricks and Conners. Today, no one knows the whole field with the possible exception of a few legislators.

The problem of "drug testing" has hurt clinical pharmacology because of a superficial and dishonest fringe. Some drug companies have fumbled, and still are fumbling, the ball. Despite my obviously superb advice, some excellent companies have persisted in treating testing as a branch of veterinary medicine in which patients are so many sheep to be sheared and dipped. This brings on such books as *The Therapeutic Nightmare* and now the problems of drug pricing.

The "quickie test" conducted by the young clinician who needs the money can no longer be tolerated. Drug evaluation is essential and must have its dignity and importance restored, with true co-operation of investigators, FDA, drug houses, the American Medical Association and the pharmacological society. We need a James Goddard in experimental therapeutics to meld these disparate parts. Even a committee would be acceptable if its decisions were not based on the lowest common denominator, which can be pretty low when people put their minds to it.

But that there is need for clinical pharmacology there is no doubt. The problem is how to create the environment in which it will flourish. Without going into the many pros and cons, let me give you my opinions based on some 40 years of rather primitive effort. The clinical pharmacologist should be a part of the medical staff of the hospital and be capable of full patient care of at least some sector of medicine, have a few beds with special nurses under his direct responsibility, especially for metabolic and physiologic studies, have special training in statistics and experimental design, provide guidance to other hospital staff members in use of drugs even though it may consist only in indicating sources of information, co-operate with other staff physicians in study

and reporting of abnormal drug reactions, be responsible for surveillance of drug costs, and be responsible for observance of patient consent and the ethical aspects of clinical experimentation in association with a peer committee of the hospital: *do not* establish a Congressional "watchdog" committee "to overlook and make sure that proper emphasis is given to adequate teaching and the application of scientific knowledge to our patients!"

Now I turn to that relatively new concern in our scientific lives, the federal Government.

## On the Federal Government and Pharmacologists

It would be an impertinence for me to try to discuss this fascinating problem in any depth. But I will introduce just a little skepticism on behalf of "The Loyal Opposition" (*Am. J. Cardiol.* 20:283, 1967). I will make it brief, with some remarks of a pH not more than 4 to 5!

First of all, medicine for the masses is now called, "delivery of health care" or "comprehensive medical care," and presumes an inherent right of everyone to the best possible care. Few would oppose this ideal as such, and I am confident that the Government and science will tend to co-operate even more closely; the problem is to inject some reality into such plans. The stage of initial enthusiasm is almost over, although there was much back scratching at a recent Washington Victory Conference for the Heart Disease, Cancer, and Stroke program. In addition, the odd notion of giving large sums of taxpayer's money for planning has been introduced.

Hiring a staff to do the legwork is hardly the way to get ideas or solve problems. It is one of the most dangerous ways I know of turning the true responsibility over to an anonymous group who too frequently impose their own views by writing the minutes and the final report of a committee.

There was a time when you were supposed to have an idea and then ask for money. How out of date can you get? The Government must come to realize that money and legislation alone cannot cure heart disease, cancer and stroke. Without creative research, not just surveys and "identification" of victims, little will be gained. Listen to the President in the Rose Garden, "Unless we do better, two thirds of all Americans now living will suffer or die from cancer, heart disease or stroke. I expect you to do something about it." Who is "you"?

Secondly, the most important innovation that the Government has made in biomedicine is without question the support of research by the National Institutes of Health and the National Science Foundation. The study section-council system was a stroke of genius that transformed research here and abroad. And despite endless Congressional investigations, little fault has been found with the system until very recently. But now the development of an effective mechanism to maintain the initial high level of appointees is imperative. I detect a growing political tendency in appointments to these vital committees and councils; yet these people are at the core of American medicine and science. Far too many of the same persons are passed from one council to the next with the agility of the Harlem Globetrotters. The system will only remain viable if new faces and ideas are regularly infused, thus preventing the formation of an "establishment." Today, we are at the crossroads in this regard.

Thirdly, the once seriously ailing Food and Drug Administration has had a series of shots in the arm with the most recent and very competent commissioner, Dr. James Goddard, adding some in the derrière. It has been overebullient, and sometimes its emotional bloomers have shown through, but the trend is right. It was long a lawyer-ridden organization with little understanding of, or by, the medical profession and was viewed with distaste by the pharmaceutical manufacturers. With a bit of maturing and the active co-operation of pharmacologists, a bright future is assured. But active participation by independent civilian pharmacologists is vital.

Fourthly, the growing trend of appointing laymen to positions of great power in determining policy and advising the President and Secretary of State is understandable, but I am not convinced of its wisdom. Certainly, Wilbur Cohen and Herman Pollack are men of high quality, but have they developed the wisdom that usually comes only from long experience in medicine or science on which to base decisions that affect us all? There must be a *better way* of seeking out and appointing professionals who might be interested.

Finally, one of the most disturbing trends is the increasing tendency of the Government to dictate terms for the conduct of research. Last year the National Institutes of Health were challenged by the White House to produce more "practical discoveries," with the implication that scientists were withholding health-giving secrets. The American people, so we were told, had come to regard health as a basic right and to demand universal quality care. Surely everyone has a right to be healthy, but the problem is as much an educational and economic as a medical one.

Probably the majority of research workers grumbled at this pressure to produce immediate practical results, but their voices were not heard. That this is deadly serious is shown by the fact that so wise and perceptive a scientist as Dr. James Shannon felt it necessary to respond not with a routine report but as a very personal concern! A special assistant, Dr. Philip Anderson, has been appointed to "determine the road blocks preventing researchers from reaching a goal, and then suggest how to beef up a program so we can get what we want sooner." The Blue Sheet reports that the National Institutes of Health may create a number of new disease-oriented committees along the lines of the breast-cancer task force, ". . . which is in full command of that cancer area—looking into grant-contract coordination, designing scientific strategy and programming research." This is research?

None of us are deluded enough to believe that the major killers—coronary disease, hypertension, stroke and cancer—have been conquered in the sense that "polio" is understood and controlled. Great progress has been made, but time for evaluating results is crucial. A perfect example of jumping the gun was the serious proposal that reserpine be made available free to the public.

Failure to understand the nature of this, in many ways, new kind of research that involves many genetic and environmental factors may well lead the nation into costly mistakes, and one of these is certainly the demand for quick practical results. Indeed, Senator Harris has suggested, as I interpret it, that new legislation be established to *assure* results. I say this with some heat because those unfamiliar with the ways of scientists do not realize that such pressures damp creative thinking, not animate it. When we splurge on space programs and the Weston 200-bev accelerator at the expense of exploring the nature of coronary heart disease, and when the press and the legislators hail to former and ignore the latter, creative research is stifled. The placing of emphasis influences research workers. *Especially* the *young, vigorous research worker* has his antennae tuned to such messages.

How much truly original work will come out of the promise of the National Institutes of Health *to capitalize* on their present knowledge? Little can be dredged up that will substantially change present medical practice. The artificial-heart program has been toned down in favor of "partial assist devices." How and when they could "assist" is still problematical. Taking over the function of the heart during the crucial first days of a myocardial infarction sounds great, but this is easier said than done and I now speak from personal experience!

The National Institutes of Health have listed what Washington likes to call "targeted" projects, which I assume they think are nearly ready for use. But listen to them: anticancer drugs; drugs to reduce atherosclerosis; improved artificial kidneys; control of renal disease; heart-assist pumps; control of hypertension (a catalogue of the wide world of research).

Even more important to me is the question how research should be administered—how an atmosphere can be created in which we "odd balls" can function effectively. Systems analysis and such procedures have their place but cannot obviate individual human creativity. Whether research workers like it or not, a report from the National Academy of Sciences will shortly appear that is supposed to establish priorities for biomedical research for the next ten years. As is said in lovely Washingtonese, the report will, "identify the main thrusts and study the interfaces." Central planning by any group of scientists has a very familiar Muscovite ring. Possibly, it is the best way to conduct research, but first we should all talk about it. A frustrating fact to the uninitiated and to the business-minded is that there is no single way to do research.

The pharmacologist can influence the course of events in many ways. One is to support the concept of a National Academy of Medicine.

## On a National Academy of Medicine

As a nonmember of most everything, I feel free to propose, criticize and generally make a nuisance of myself.

I have long been deeply concerned with the growing estrangement between the Government, the American Medical Association and the American public. We no longer understand one another, and instead of a dialogue, a name-calling contest has developed. This is impinging tangentially on pharmacologists because of investigations such as those of Senator Kefauver and now Senator Nelson. Involvement of pharmacologists can only become deeper and could become more painful.

These alienations have many causes but I have a specific proposal for one of them. An uninvolved person who needs an authoritative opinion has nowhere to go. A dispassionate opinion is rare because of interference by power, money, prejudice, status and often sheer mediocrity. The calm voice of

wisdom is most likely to be heard when a man is beholden to no one.

*Science* has long had an organization that in many ways fulfills this need. The National Academy of Sciences was created to recognize continuing creative research and to provide counsel to the nation as it is called upon. There are sections on physiology, biochemistry, microbiology and pathology, and these are constituted of a handful of men. But the great field of medicine as a whole is unrepresented.

Three years ago I made editorial appeal for the creation of a National Academy of Medicine. Sophisticated scientists and physicians know what such an Academy should do. I would have it broadly based to include the basic sciences directly concerned with medicine as well as social and behavioral aspects, and would not require an M.D. degree for admission.

I am glad to report that the idea has received broad acceptance and is being explored with the National Academy of Sciences. The show is patently on the road and a worthy instrument for the best interests of medicine and the public should emerge.

## On Science Writers, The Press and Pharmacology

To turn to public images, I wonder if physicians and pharmacologists are fully aware of how important science writers and the press have become to medicine. Twenty years ago we disparaged them, but with the granting of federal funds and the deep involvement of the Government in medicine and research a large and frightening change has occurred: now we want all the publicity we can get. But more importantly we must take the public and the Government into our confidence to show them the true nature of the difficult problems we face, as illustrated by the recent airing of the problem of patient consent.

Let me quickly explain that there is a large difference between *educational reporting* of medicine and *publicity* largely to create "public images." I see nothing but good coming from giving the public a better understanding of science and medicine. Even changes in the law may well depend on an informed public. We should not be an arrogant, inarticulate new priesthood. But "do-it-yourself" television courses in living-room surgery and the anticancer breakthroughs are not the way to do it. These create celebrities but leave the mind sterile.

Not long ago science writers as such did not exist. Do you realize that Kaempfert and Lawrence, of the *New York Times,* in the early twenties were among the first full-time science writers? They have grown into a remarkable effective group. Who could not but admire such fine organizations as the Council for the Advancement of Science Writing and the National Science Writers' Association? But occasionally they revert to yellow journalism. Their reporting of the artificial-heart experiments and of DMSO were, to my mind, a disgrace. They want to be considered as professionals just as they should be. But to do so they must exercise judgment both about a person and about his work before they undertake to educate and inform the public. To my surprise, some of my good and respected friends among the science writers disagree with me on this point.

I am afraid I cannot yield if only because I both respect science writers as professionals and see the vital need to have them as a part of the medical and research professions. We must learn to live together with mutual understanding and trust. But we must pick with care those we support because praise makes good men better and bad men worse. When I look around and see such men as Al Blakeslee, Al Rosenfeld, Art Snider, Gil Cant, Jerry Bishop and Ray Bruner, I realize that we have many fine ones to choose from.

I have only to remind the reader of the recent donnybrooks with the FDA and various humane societies to underscore my words.

## Conclusions

Let us remember that pharmacologists are a vital part of the woof, warp and web of medicine and of science. This new genre has deep ethical responsibilities, and a few of us think even transcendent and religious as well; for the simple reason that until we all agree on the meaning of life, a unified ethic cannot be constructed.

But I shall not press these issues. To me the woes and ills of man are not wholly material, although science has certainly added to their number. Almost everywhere in the world today there is violence and revolt. The scientific community must find ways to help return the world to sanity. Though numerically small, we can have a disproportionate influence if we plan and work at it. With great subtlety through their potions, the pharmacologists have learned to change man's material environment. They must now learn to deal with the meaning of these changes in terms of the individual human being. There is nothing man fears more than sickness or the loss of his life. Pharmacologists are a vital part of that small band of men who labor to prevent both. Think, think what this means!

# HEREDITY IN DIABETES MELLITUS

*Arthur G. Steinberg, PhD, Western Reserve University, Cleveland, Postgrad Med 43(4):145–147, April 1968. "Reprinted from Postgraduate Medicine*


*Precisely who in a family will inherit diabetes and at what age puzzles geneticists. The autosomal recessive gene hypothesis has proved useful in counseling patients with a family history of diabetes.*

A character that occurs more often among the relatives of an individual with the character than in the general population *in the absence* of environmental factors that can explain the familial concentration has an important genetic component in its determination. There is universal agreement that diabetes mellitus fulfills this criterion and that heredity plays an important role in determining susceptibility to this disease.

Earlier in this series Becker described the simpler patterns of inheritance. These patterns may be recognized with relative ease if the character is easily diagnosed, is congenital or appears in early childhood, and develops in all persons with the appropriate genotype. However, diabetes does not fit these patterns. It is often difficult to diagnose, it may develop at any time from birth to old age, and it often fails to develop in persons with the genetic predisposition (failure of penetrance).

Thus, analysis of the pattern of inheritance in diabetes is most difficult. I have discussed this problem in detail elsewhere. The best working hypothesis appears to be that homozygosity for an autosomal recessive gene causes susceptibility to diabetes. This paper will explore the consequences of this assumption in genetic counseling.

## Genetic and Environmental Factors

It is necessary to distinguish between genetic predisposition, which is inherited, and frank diabetes, which is the clinical expression of genetic predisposition. An individual's genotype is determined at the time of fertilization. Clinical diabetes may not occur until some decades later. Hence diabetes results from the interaction of inherited predisposition and environmental factors.

Assuming recessive autosomal inheritance of susceptibility to diabetes and allowing *d* to represent the recessive gene and *D* the dominant gene, matings that may give rise to diabetes and the proportion of susceptible children from these matings are as follows:

Normal x normal (*Dd* x *Dd*) One-fourth
Normal x diabetic (*Dd* x *dd*) One-half
Diabetic x diabetic (*dd* x *dd*) All

In practice we recognize a "diabetic family" because a member is diabetic. If both of the patient's parents are nondiabetic, they probably have the genotype Dd, and we may predict that one-fourth of the patient's siblings will be genetically liable to the disease. If one parent is diabetic and the other is nondiabetic, one-half of the patient's siblings will be genetically liable regardless of the sex of the diabetic parent. Finally if both parents are diabetic, all of the patient's siblings will be liable to diabetes.

We are still unable to detect *Dd* individuals except by genetic history. Similarly we cannot satisfactorily determine *dd* individuals before frank diabetes develops. Therefore we cannot predict precisely the occurrence of susceptibility to diabetes among the offspring of diabetics who have not yet had a diabetic child. Nevertheless, we can estimate the probability of the occurrence of genetic liability to the disease among offspring and other relatives of diabetics. The predictions summarized in table 1 are based on an estimated frequency of the *d* allele of *22* percent.

Various studies have shown that the age at onset of diabetes is earlier in a child than in his diabetic parent in 60 to 65 percent of parent-child pairs. The mean age at onset in the child is about 20 years less than that in the parent. This phenomenon is referred to as anticipation. Some workers have claimed that anticipation has a biologic basis and that the age at onset of diabetes in the parent can be used

TABLE 1.—*Genetic Liability to Diabetes as a Function of Disease in Various Relatives*

| Probability of Diabetes* | Diabetic Relative(s) |
|---|---|
| 20 percent | 1. First cousin. 2. Aunt or uncle. 3. A grandparent. 4. Both paternal or both maternal grandparents, or a parent. |
| 30 to 40 percent | 1. One maternal and one paternal grandparent. 2. One parent and a first cousin via the nondiabetic parent. |
| 50 to 80 percent | 1. One parent and a sibling of the nondiabetic parent. 2. One parent and a parent of the nondiabetic parent. 3. One parent and a sibling and a parent of the nondiabetic parent. |

* Within each group the probability is lowest when the affected relative(s) is of No. 1 and greatest when the affected relative(s) is of the highest number given.
From Steinberg, table 5.

to predict the age at onset in the child as well as the age at which he will no longer be susceptible.

Unfortunately the assumption that anticipation is a biologic phenomenon is incorrect. Investigation has shown that the age at which the parent became diabetic does not influence the age of onset in the child. The observed relation between the ages at onset in the parent-child pairs is a statistical phenomenon and has no predictive value. This is true regardless of the sex of the diabetic parent.

Some workers have also claimed that pregnancy is one of the environmental factors that cause frank diabetes in genetically liable persons and that for a given age interval the prevalence of diabetes increases with increasing parity. The studies on which these claims were based are not entirely satisfactory. A study of all women in an American Indian tribe living on a reservation in Arizona failed to confirm an association between parity and the prevalence of diabetes. The average weight increased with increasing parity in the women in the earlier studies but not in the Indian women. Thus, it seems reasonable to conclude that the observed association in the earlier studies was between diabetes and obesity rather than between diabetes and parity.

As I stated earlier, the genetic basis of susceptibility to diabetes remains unsolved. The autosomal recessive gene hypothesis is simply a satisfactory working hypothesis. Solution of this problem requires a better definition of diabetes and improved diagnostic tools. While not essential for determination of the pattern of inheritance, the ability to detect prediabetic persons would simplify the problem and aid in genetic counseling.

I have refrained from stating what advice diabetics should be given about childbearing because I believe interpretation of the risks involved can best be done by patients in consultation with those who know and understand them. The interpretation will vary from patient to patient.

(The references may be seen in the original article.)

## THE EARLIER DIAGNOSIS OF STOMACH CANCER

*James Richard Hoon, MD, Sheboygan, Wis., Arch Surg 98(2):144–149, Feb 1969.*

In the United States, diagnosis of early gastric cancer is, for the most part, grossly inadequate despite availability of new and improved diagnostic means. One of the several reasons for this, in the face of the very poor results in treatment for gastric cancer, is that it has been fashionable of late to point out that the incidence of gastric cancer in the United States is reducing (meaning that it may now be relatively ignored). However, among causes of death from cancer projected for 1968, stomach cancer ranks fifth, behind lung, breast, colon, and pancreatic cancer, and ahead of rectal cancer. Concerning importance of early diagnosis of stomach cancer, it should be sufficient to note that the five-year survival of those with localized gastric cancer in the United States is 40 percent, whereas with regional involvement, a five-year survival of only 12 percent results. These figures alone establish quite a case for early diagnosis.

In Japan, the incidence of deaths from gastric cancer is at the highest level of all cancers in that country. Facing the problem, the Japanese have produced significant advances in techniques for diagnosis of stomach lesions. Japanese roentgenologists have advanced the techniques of double contrast and mucosal pattern studies with x-ray films of the stomach lesions. Gastric cytology in Japan has been at a high degree of accuracy for years. Intragastric photography has been farther developed in Japan than any place elsewhere in the world. This has been made possible largely through the agency of the gastrocamera. Modifications of this instrument have included the adaptation of a fiberscope for observation of the areas to be photographed and of devices to increase mobility of the camera within the stomach. Biopsy of gastric mucosa has reached a high stage of technical ability now suitable for wide clinical use. Again, this has been done mostly in Japan.

Although the gastrocamera was placed in clinical use in 1950 in Japan, it was not until 1963 that it was

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successfully introduced in the United States by Yoshio Hara, MD, of the Niigata Cancer Center, working on exchange at the University of Wisconsin Cancer Research Hospital. The gastrocamera was within months in operation at the University of Wisconsin Gastroenterologic Department, and at Columbia University and the Sheboygan Clinic. By October 1967, 11,000 gastrocameras had already been placed in operation in Japan; 350 gastrocameras were by then in operation in the United States as reported by K. Oneda (personal communications, Oct 30, 1967). It is unfortunate that the combined barriers of language, culture, and customs have delayed introduction of the gastrocamera in the United States from 1950 to 1963.

While the incidence of gastric cancer is reducing in the United States, the rate of death from this lesion remains high. One factor is the delay in identifying the lesion. It is clear that late diagnosis usually dooms the patient regardless of what modern techniques are used in combating stomach cancer. Early diagnosis and, hence, probably earlier treatment of the disease is a means of possibly improving results in gastric cancers now.

## Methods and Instruments

The gastrocamera (GTV) is a versatile instrument with a high degree of photographic excellence within the stomach. Its principal advantage over other gastric photographic devices is that the films, lens, and light source are within the stomach and the camera does not merely photograph through a fiberoptic device from without the body. It is guided to position by the light reflex of its flashing lamp seen through the stomach wall. The gastrocamera can photograph almost every part of the stomach and is especially able to photograph those parts which include the majority of stomach cancers. A recent modification (GTV-a) has a device to increase mobility of this camera within the stomach.

Addition of a fiberscope to the gastrocamera has added direct visualization of suspected areas of the stomach in the gastrocamera (GTF) with fiberscope. This instrument also has had a recent modification increasing mobility of the distal end making a new instrument (GTF-a). This has been termed at the May 1967 meeting of the American Society of Gastrointestinal Endoscopy as the best single device for intragastric photographic diagnosis.

Gastric cytology and gastric biopsy may be performed under direct visualization of a lesion, permitting either direct washing against the suspected area or a biopsy of the area with the Japanese-developed gastrofiberscopes for biopsy. These are not instruments which are easily used, but in expert hands can give good results.

With these tools one may, following x-ray studies of the stomach, obtain gastroscopic impressions of the stomach through the fiberscope, direct photographic studies of the mucosa through the gastrocamera, and cytology or biopsy studies of the stomach. There is, however, a more difficult problem, that is, the obtaining of earlier referrals of subjects with minimal stomach complaints suitable for these examinations.

## Results

There is no great problem in identifying far-advanced gastric cancer by intragastric photography or by other means. Identifying early pathologic conditions by photographs of a gastric mucosa as "benign" or "malignant" is considerably more difficult. Some of these lesions must perforce, be labeled "probably benign," "probably malignant," or "equivocal."

At the Japan National Cancer Center, Tokyo, in operation since 1962, an enthusiastic search for early gastric cancer had found well over 200 early stomach cancers through 1966 as reported by M. Kuru, MD, (personal communication, 1966). "Early gastric cancer" has been defined by the Japan Gastroenterologic Endoscopy Society in 1962, as "a carcinoma of the stomach, the invasion of which is limited to the mucosa and submucosa." To qualify, these must be confirmed by the pathologist. This is after the clinical diagnostic procedures of x-ray studies, gastrocamera examination, cytology, and possible biopsy, where indicated. These are tough standards to meet, and the finding of a qualifying case is of great significance in a country where carcinoma of the stomach in both sexes is the leading cause of malignant disease in death.

At the Sheboygan Clinic, March 1964 to December 1967, 637 patients have been examined with the gastrocamera. Of these 136 were for experimental purposes, leaving 501 clinical examinations. Twenty gastric cancers have been photographed since beginning gastrocamera photography in Sheboygan in March 1964 (5 percent of the clinical examinations). Of the 20 cancers, eight were not identified by prior x-ray studies. In one patient, severe polypoid gastritis was found by gastrocamera in several examinations. However, by observing a slight enlargement of a gastric polyp in this patient in a series of

x-ray films, the roentgenologist cautiously suggested the malignant nature of one of the polyps. This proved at surgery to be an early gastric cancer, as defined by the Japanese.

Report of Cases

Case 1.—This was the first gastric cancer diagnosed in a 69-year-old woman by intragastric photography at Sheboygan. The patient had three gastric x-ray films: Jan 8, 1964 (diagnosed normal); Feb 8, 1964 (diagnosed hypertrophic gastritis); and Aug 14, 1964 (a normal stomach). On Aug 18, 1964, gastric analysis revealed no free hydrocholoric acid. Malignant undifferentiated cells were found on gastric cytology on that date (the pathologist's first "positive" gastric cytology). On Aug 24, 1964, a gastrocamera examination was made demonstrating a malignant ulcer at the angle of the stomach. This patient was operated on on Aug 28, by another surgeon, and found to have a carcinoma as described. Unfortunately, there was some regional spread. The patient died Oct 23, 1965.

Case 2.—In an 89-year-old woman, x-ray studies revealed "some irregularity in the antrum, possibly an ulcer in the antrum; malignant growth cannot be excluded." Gastrocamera revealed extensive carcinoma of the midantrum although there appeared to be ample gastric mucosa, apparently uninvolved, above the large lesion. The patient was not subjected to surgery by the referring physician. She died on Feb 15, 1966.

Case 3.—In an 81-year-old patient, x-ray studies revealed "a stiffened area without definite lesion but suspicious of neoplasm of stomach." By gastrocamera examination, the patient was found to have carcinoma of the stomach type 2c plus 2a (superficial type with elevation and slight depression). An exploratory operation was performed and the patient was found to have hepatic metastases.

Case 4.—In a 59-year-old woman, x-ray films showed a large gastric ulcer at the midlesser curvature, January 1967. On Jan 4, 1967, gastrocamera (GTV and GTF) examinations were made. The large gastric ulcer at the angle on the lesser curvature was deemed "probably malignant." Cytology from smears made from the tips of the cameras found no malignant cells. The referring physician elected a short period of medical treatment. On Jan 17, 1967, at x-ray film examinations the gastric ulcer appeared somewhat smaller than at the previous examination. On Jan 18, gastrocamera examination (GTF) again revealed the ulcer, again calling it "probably malignant." The patient was operated on by another surgeon on Jan 24, 1967, at which time the ulcer at surgery appeared benign with a deep crater 2 cm in diameter. The pathologist termed the ulcer grossly a benign ulcer. Initial microscopic sections also were benign. However, the suspicious pathologist, on cutting more sections later, found one small focus of adenocarcinoma at one point on the wall of the ulcer. There was no deep penetration, no involvement of the base of the ulcer, nor of the peritoneum, nor the regional lymph nodes. The patient remains well (December 1967). In the opinion of the pathologist, this would be classified as "a carcinoma arising on the basis of preexisting ulcer, a rare finding." It also may be classified as an early gastric cancer.

Case 5.—In a 63-year-old man, x-ray studies revealed "a question of lesion at the esophagogastric juncture" but no diagnosis was made. A gastrocamera (GTV and GTF) was attempted on May 19, 1966. It was not possible to make retrograde films with the camera (GTV) because of pain on the part of the subject on retroverting the camera. However, the camera GTF obtained good close-up pictures of the esophagogastric juncture demonstrating a probably malignant lesion at this level. An operation by another surgeon performed on the following day revealed no evidence of carcinoma in the area, and only on gastrotomy could a very small "benign" ulcer be felt at the esophagogastric juncture. No resection was performed. Regretfully, later in the same day, cytology previously taken was reported as showing suspicious cells for malignancy. A stormy postoperative course with pneumonia and wound dehiscence precluded any early surgery. A gastrocamera examination on Aug 6, 1966, again revealed a high suspicion of a neoplastic lesion at the esophagogastric juncture. At this time it was not possible to pass the camera (GTF) because of apparent obstruction at the esophagogastric juncture. The camera (GTV) was passed with some difficulty and photos were classed only "fair." On March 18, 1967, the camera (GTV) was passed again, finding most of the photos obscured by bloody mucus and only on three or four frames was some very irregular mucosa seen confirming the x-ray film impression (now) of neoplastic tumor at the esophagogastric juncture. An exploratory operation was performed by the patient's surgeon on April 4, 1967, and inoperable carcinoma of the cardioesophageal position of the stomach was found. The patient is still alive (December 1967) and able to take liquid food.

This patient, in my opinion, probably had an early gastric cancer when first photographed.

Case 6.—This 60-year-old man had a partial gastrectomy for benign ulcer 20 years before his gastrocamera examinations. He had had a 30 lb weight loss in the three months preceding gastrocamera examinations. X-ray studies in December 1966 revealed an apparently normal postgastrectomy stomach. Gastrocamera examination on Dec 12, 1966, showed a gastrojejunal marginal ulcer, postgastrectomy, suggestive of malignancy. This patient was rephotographed on Jan 4, 1967, with a finding of probable carcinoma in a postgastrectomy stomach. On Jan 6, exploration revealed extensive regional involvement of gastric carcinoma.

Case 7.—This patient, a 73-year-old man, complained only of epigastralgia. X-ray studies revealed marked antral gastritis, with a possibility of infiltrating neoplastic lesion suggested. The gastrocamera (GTF) demonstrated on Nov 15, 1967, a malignant gastric ulcer in the immediate prepyloric region of the greater curvature. Gastric biopsy was tried but was not deemed satisfactory. The biopsy material obtained was found to be benign. On the basis of the gastrocamera photographs, an exploratory operation was performed Nov 28, 1967, disclosing neoplastic adenocarcinoma of the stomach with penetration through the peritoneal surface and with metastases to the regional lymph nodes.

Case 8.—This patient, a 72-year-old woman, had, in December 1963, a carcinoma of the descending colon (which had spread locally) removed, and a carcinoma of the cervix and carcinoma of the uterus (both with apparent local spread), also removed. She has been on a regimen of fluorouracil since that time. At operation for acute cholecystitis in 1964, no apparent carcinoma was found within the abdomen. Also in December 1963, an x-ray film of the stomach was obtained disclosing a small rounded lesion slightly more than 1 cm in size in the distal end of the stomach, regular and sharply outlined. It was diagnosed as a small myoma or polyp. A gastrocamera examination on Aug 7, 1965, revealed very marked multiple polyposis of the stomach, of the hypertrophic gastritis type, with marked gastritis.

Having continued epigastralgia, a repeat gastrocamera examination on Dec 14, 1966, again revealed hypertrophic gastritis with marked superficial gastritis and multiple small, flat, broad, polypoid lesions along the greater curvature, deemed polypoid gastritis. She responded fairly well to medical treatment. Fluorouracil administration was continued. On Oct 6, 1967, an x-ray film of the stomach revealed the polyp in the lower antrum to have enlarged somewhat. Gastrocamera examination on Oct 7, 1967, revealed only the superficial gastritis and marked polypoid gastritis previously seen. The polyp itself was not differentiated from the other polypoid lesions in this area. Because of the continued epigastralgia and especially the "slightly enlarging" polyp, a gastric resection was performed on Oct 11, 1967, including the distal 50 percent of the stomach. The specimen, in addition to polypoid gastritis, contained the polyp seen at x-ray studies and found to have a long, slender stem and to be smooth and rounded on its surface. On section, the surface mucosa of the polyp was benign, but at the center of the polyp and just beginning progression down the stem, it was adenocarcinomatous. There was no evidence of carcinoma in the wall of the stomach or elsewhere. This is an early gastric cancer found fortuitously and with an assist from the roentgenologist.

Case 9.—This patient, a 69-year-old woman, complained of long-term epigastric discomfort. Many previous surgical procedures had been performed on her, including a gastroenterostomy 15 years before the present examination. X-ray studies revealed a normally functioning stomach, postgastroenterostomy, with no evidence of an active lesion in the stomach at that time. On March 31, 1966, gastrocamera (GTV) examination revealed a healthy-appearing anastomosis, but at the angulus, a thickness of the posterior aspect of the angle was noted with some local redness of the mucosa suggesting a lesion or ulcer either seen on the edge or incompletely visualized. A repeat examination on April 21, 1966, with the camera (GTF) demonstrated a small ulcer on the upper lesser curvature adjacent to an area of blood-streaking near the thickened, suspicious area noted on March 31. The diagnosis was ulcerative lesion, high on lesser curvature with possibility of malignancy. Surgical exploration revealed a pancreatic cancer invading the wall of the stomach at the point seen by gastrocamera.

Case 10.—The case of this 76-year-old man demonstrates the value of the combined approach of various means in diagnosing gastric lesions. This patient had an x-ray film diagnosis of malignancy of the antrum of the stomach. A gastrocamera examination revealed a benign ulcer of the greater curvature of the stomach. Biopsies taken from this region was found to be benign. A medical trial subsequently, with follow-up gastrocamera examinations, demon-

strated healing of his gastric ulcer. It must be remembered, however, that biopsies diagnosed as "benign" are of little significance, and that only a diagnosis of malignancy by biopsy has credence in general.

## Comment

Until we find some chemical or immunologic method of preventing or overcoming cancer of the stomach, it appears that our hope of cure of the condition depends on earlier diagnosis and earlier, not wider, surgery. A considerable series of advances in earlier diagnosis of gastric cancer have been made by the Japanese, not because they are better physicians than we in the United States, but because they have a better reason in that gastric cancer in Japan is the leading cause of deaths from malignancy in both men and women. In the United States it only ranks fifth.

Earlier diagnosis of stomach cancer may rest primarily in that group of patients who have sufficient symptoms to require or obtain a gastric x-ray film study, which is then interpreted in good hands as "normal or essentially negative" for significant lesions, or just plain "suspicious." In the series of 637 subjects at the Sheboygan Clinic, I have found a significant number of lesions in patients with symptoms who have, however, "normal or negative" gastric x-ray film results. For example, of 68 patients with gastric ulcer identified with the gastrocamera, 23 had "normal or negative" gastric x-ray film findings. Four of ten polyps seen at gastrocamera examination were also in this category. Most significant is the finding of eight gastric cancers with intragastric photography in which the diagnosis was not made by well-qualified roentgenologists in a group of 20 patients with gastric cancers examined in Sheboygan. In one case, stomach cancer was suggested by x-ray film examination of a slightly enlarging polyp, demonstrating the value of a combined approach to the diagnosis. (Patients with advanced cancers are not usually subjected, in Sheboygan, to intragastric photography at the present time.)

Steady progress in improving the design of gastrocamera devices, and the search for optimum photographic conditions with gastrocameras in considering minute changes in stomach mucosa, such as minimal variations in mucosal color, are examples of Japanese urgency in the detection of early gastric cancer. The gastrofiberscope for cytology has improved the results of gastric cytology, now permitting direct washings against suspected lesions. The development of biopsy gastrofiberscopes makes possible practical gastric biopsy under direct vision. These instruments are somewhat complicated and require rather delicate handling. Both Hara and Kasugai emphasize the problems in gastric biopsies and the need for considerable training in mastering the technique. However, they find in the combined employment of the presently available methods of modern x-ray film diagnosis, intragastric photography, cytology, and biopsy, an increased accuracy of diagnosis with the stomach to "almost 100 percent."

Masaru Kuru writes that the diagnostic methods—x-ray film, gastrocamera, cytology, and intragastric biopsy—have both strong and weak points, individually. They are, however, complimentary so that the combination of these methods can more fully satisfy the desire to detect carcinomas of the stomach at the earliest stage. This has proved most fruitful at the Japan National Cancer Center. Kuru finds that more care in accurate diagnosis of stomach lesions can permit a more logical approach to therapy in the patients.

## Conclusion

In view of the poor general results in treatment of gastric cancer, it appears that more aggressive search for early and possibly curative cases is indicated in the United States. Whether delay in diagnosis is due to the patient's delay in seeking advice or to a lack of diligence on the part of the physician in using or advocating use of the newer diagnostic methods, here described and now available, can possibly be argued. But it is known that factors leading to late diagnosis could be overcome by using the methods described and earlier referrals for these examinations. With diagnosis made and definitive treatment accomplished without unseemly and too often fatal delays, we should look for improvement in our survival figures.

(The figures and references may be seen in the original article.)

# SERUM URATE LEVELS: A REAPPRAISAL

*Frank R. Schmid, MD and Joseph T. Tesar, MD, Resident Physician 14(12):45–50, 88, 89, 94, December 1968.*

Many complexities surround the serum urate value. Some of them have been with us for years, but many more have been introduced more recently by the widespread use of drugs. In the interest of accurate diagnosis and effective treatment, a sure knowledge of the factors that influence serum urate values is essential.

Interpretation of an elevated level of serum urate* poses problems for the physician since an increasing number of situations are being encountered in which values obtained seem to be at odds with the clinical impression. One of the most common sources of confusion stems from the patient's use of drugs that influence urate metabolism or excretion. Other factors that must be considered are the methods employed in the urate determination and an increasing number of disease states, besides classical gout, that are associated with changes in serum urate values.

Now as always, a patient with classical features of acute gouty arthritis offers little difficulty in diagnosis. The sudden onset of a single, or perhaps two, painful joints in an adult male arouses suspicion at once. A specimen of synovial fluid which reveals urate crystals free in the fluid or ingested by polymorphonuclear white cells is another clue to the diagnosis. The demonstration of such crystals in joint fluid provides unequivocal evidence of gout. The results of this bedside procedure are available almost immediately, long before the laboratory report of an elevated serum urate value is returned.

However, patients with atypical arthritic syndromes or without joint disease who present with elevated serum urate levels require further evaluation. Indeed, the numbers of such patients are substantial. In these circumstances, the physician must consider the various factors besides gout that influence serum urate values. An illustrative case history will serve to highlight this approach.

For several years, a 49-year-old male has noted occasional episodes of pain in the neck and lower back and, on several occasions, pain in his knees. No definite redness or swelling has occurred. At other times, he has continued an active productive life. On the occasion of one such episode, a urate determination was performed. The result of the test was 7.9 mg percent.

This serum urate value might lead the physician to consider the diagnosis of gout. However, the pattern of the illness is not entirely compatible with gout, but more likely would be caused by other diseases such as osteoarthritis, herniation of intervertebral discs with postural strain on his knees, ankylosing spondylitis, and so on. In fact, had the urate value been normal it is likely that the diagnosis of gout would have been discarded.

Thus, before he accepts the diagnosis of gout, the physician should ask two questions.

Are there further confirmatory tests that can be made that would substantiate the diagnosis? The demonstration of urate crystals in synovial fluid from the knee would give an unequivocal answer. A brisk response to treatment by colchicine would be very suggestive of gout.

The second question that should be asked is whether the elevated serum urate value could be ascribed to factors other than gout.

It is the purpose of this review to briefly discuss what is currently known of these various factors that influence serum urate values.

## Age and Sex

A male at age 49 would be an ideal candidate for the development of gout. Gout rarely develops before the early twenties in men and before the onset of the menopause in women. This critical observation is based upon a hormonal dependence of the serum urate value. There is a gradual rise with age which reaches a higher level for males than females and is sustained over most of adult life. Thus, before the age of puberty, children of both sexes have similar levels of urate in the range of 4.0 mg percent. After puberty, the curves for males and females diverge; males achieving an average level of 5.0-5.5 mg percent, a full milligram higher than the female group. This gap is narrowed somewhat, although never quite closed, following the menopausal period.

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Dr. Schmid is Associate Professor of Medicine and Chief, Arthritis and Connective Tissue Disease Section, Department of Medicine, Northwestern University Medical School.

Dr. Tesar is a postdoctoral fellow in the arthritis and connective tissue disease training program at the same institution.

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* Urate, rather than uric acid, is the form in which this substance exists within serum and body fluids and in tissue deposits as tophi. In the urine, it is converted to uric acid.

The point at which a certain value of serum urate can be considered definitely abnormal varies somewhat from laboratory to laboratory (see section below), but a figure in excess of 7.5-8.0 mg percent is well above that found in a population of healthy individuals. In the interval between these high values and the normal mean value, one is sometimes hard pressed to decide the significance of the value. Patients who develop gouty arthritis occasionally present with such levels and sometimes even with levels under 6.0 mg percent, but this is rare. However, if urate determinations are repeated in the next several months or years, as was done in an epidemiological study in Framingham, Massachusetts, such individuals will be shown to have higher, more diagnostic values. On the basis of ongoing studies of this type, the generalization can be made that gout develops in a person who has a pre-existing elevation of serum urate, often for a long period of time.

## Race

In general, no race is spared the exquisite misery of gout. The same applies incidentally, to one's station in life: wealthy or not, gout is no discriminator. However, careful studies have disclosed a somewhat higher incidence of hyperuricemia and gout in certain ethnic groups. No unusual distribution seems to exist for various Caucasian or Negro groups, but Filipinos, the Maoris of New Zealand, two groups from the Mariana Islands, and the Blackfeet tribe of American Indians all have a greater number of individuals with hyperuricemia. Perhaps, as further studies of this type are carried out, a similar increased frequency will be found for other selected groups. The clinical implications of this will vary depending on the location of one's practice, but one's index of suspicion for hyperuricemia can be raised when confronted with individuals of certain ethnic groups.

TABLE 1.—*Drugs Known to Affect Urate Metabolism**

| Increased Serum Urate Values | Decreased Serum Urate Values |
|---|---|
| Salicylate (low dosage) | Salicylate (high dosage) |
| Thiazides | Probenecid |
| Furosemide | Sulfinpyrazone |
| Ethacrinic acid | Phenylbutazone |
| Pyrazinamide | Chloroprothixene |
| | Coumarins |
| | Acetohexamide |
| | Corticotropin |
| | Corticosteroids |
| | Allopurinol |

* Although many drugs cause either urate retention or urate excretion depending on the dosage level used, the effect of the drug that is cited is the one expected in ordinary clinical practice.

## Drugs

Of all the factors that affect urate metabolism, none has assumed greater importance or caused more confusion than drug ingestion. A long list of drugs have been identified as agents that influence urate levels. For this reason, it would be preferable to obtain blood specimens for serum urate values only from patients who have not taken medication for a period of at least 3-4 days, and preferably somewhat longer. However, in actuality, such a condition usually is not possible in medical practice. It is a rare person who, when ill, does not avail himself of medication. Therefore, the physician must obtain a complete history from the patient regarding his use of drugs. It is especially critical to inquire about patent medicines. Most patients do not regard ingestion of several aspirin tablets as "medication," yet even such a small dosage prior to the test will change its values.

To understand how drugs change serum urate value requires a brief review of the pathway of urate metabolism. Drugs can be grouped according to their action upon various points of this pathway. Also, some disease states as will be discussed below have similar effects.

*Uric Acid Metabolism and Excretion*—Uric acid is synthesized from amino acid precursors: aspartic acid, glutamine and glycine, and from carbon sources: formate and carbon dioxide. Nucleotides from the breakdown of ingested nucleic acids contribute in a minor degree to the synthesis of uric acid. Approximately 750 mg of urate are synthesized and excreted daily. Two-thirds of this amount is eliminated through the kidneys and the remaining third by the intestinal route.

In the kidneys, urates are filtrated through the glomerulus, but 90 percent or perhaps even more of that amount is reabsorbed in the tubule. Urate is also secreted into the tubule, and most of the uric acid actually found in the urine represents this secreted fraction. Weak organic acids (lactic acid, hydroxybutyric acid, salicylic acid) compete for this secretory mechanism and thus may cause urate retention when present in serum.

*Salicylates*—Doses of 1-2 gm of acetylsalicylic acid per day are effective inhibitors of urate tubular secretion, thus hyperuricemia results. However, salicylates in much higher doses (4-6 gm per day) paradoxically are uricosuric, since at this level they also interfere with the reabsorptive pathway, the net effect being hypouricemia. It should be recalled that many commonly used preparations contain salicylates. A

partial list includes APC, Anacin, Bufferin, Alka-Seltzer, Coricidin, Darvon compound, Empirin compound, Percodan, Fiorinal, Zactirin, and Robaxisal.

This paradoxical effect is not unique to salicylates. It seems to be true for many of the drugs that effect renal handling of urate. Usually if the compound is given in a smaller dosage, the secretive path is blocked first, but at larger doses both the secretive and reabsorptive pathways are blocked. It is perhaps more evident for salicylates since the dosage range in which these two effects are encountered is well within that usually employed clinically. With other drugs, the commonly used dosage range is only in a zone that causes one or the other of these effects, but not both.

*Thiazide Diuretics, Furosemide, and Ethacrinic Acid*—These fast-acting diuretics all inhibit tubular secretion of urates, thereby leading to hyperuricemia. Since their continued use may be required in certain gouty patients, it is well to know that the hyperuricemia induced by thiazides can be counteracted by giving probenecid or sulfinpyrazone. This is probably true also in hyperuricemia induced by furosemide or ethacrinic acid.

*Pyrazinamide*—This drug used in the treatment of tuberculosis has been shown to have a hyperuricemic effect in a 3 gm daily dosage. Pyrazinamide markedly inhibits renal urate clearance.

*Probenecid and Sulfinpyrazone*—Both drugs are used for their potent uricosuric effect, the result of inhibition of the tubular reabsorptive mechanism for urate. Their main indication is treatment of the hyperuricemia of gouty arthritis. When used on a long-term basis they are able to normalize the markedly increased urate pool of such patients, provided the renal function is adequate. Probenecid is a sulfonamide derivative usually given in a dose of 0.5-2.0 gm daily. Sulfinpyrazone is a phenylbutazone derivative and is effective in a dose of 400-800 mg per day. Neither one has an anti-inflammatory effect and, because of this, is not a suitable agent for relief of pain and swelling of acute attacks of gouty arthritis.

*Phenylbutazone*—This drug, although structurally a close relative of sulfinpyrazone, has only weak uricosuric properties in the ordinary dosage of 300-400 mg per day. When large amounts are given, this effect may be more marked.

*Chloroprothixene*—Unexpectedly, some common drugs used in diverse clinical situations markedly increase the renal clearance of uric acid. Healey first described the uricosuric properties of such a drug, chloroprothixene, which is primarily a tranquilizer. The uricosuric effect occurs with daily doses in excess of 50 mg. A similar circumstance was found in the case of zoxazolamine, a drug no longer on the market because of toxicity. It was used as a muscle relaxant for several years until its potent uricosuric properties were discovered.

*Coumarins*—Ethyl biscoumacetate has been shown to have a potent uricosuric effect, perhaps equal to that of probenecid. It operates upon the renal tubular mechanism. A similar but less potent effect was reported for dicoumarol (500-750 mg/day) in 40 patients treated following myocardial infarction.

*Acetohexamide*—A substance recently introduced in the treatment of diabetes mellitus, it has the capacity to lower blood sugar as well as urate levels. Yü et al reported an average 33 percent increase of urate excretion following a 0.5 gm daily dose of acetohexamide. Tolbutamide, however, has no such effects.

*Corticotropin and Corticosteroids*—Corticotropin and corticosteroids have anti-inflammatory as well as uricosuric properties. Several workers have shown that larger therapeutic doses of ACTH will induce a decrease in serum urate levels.

*Allopurinol*—Allopurinol, a purine derivative recently introduced in the therapy of gout, decreases urate synthesis. It is a competitive inhibitor of xanthine oxidase, an enzyme involved in formation of urate from xanthine. In doses of 300-800 mg daily it is an effective hypouricemic agent. Its particular value is in hyperuricemia associated with renal damage, in patients with renal stones, or in patients with high nucleic acid turnover rates, as in leukemias during treatment with cancer chemotherapeutic agents.

*Combination of Salicylate with Uricosuric Drugs*—For reasons not completely understood, the use of salicylate, whether in a small or large dosage, negates the uricosuria induced by probenecid and sulfinpyrazone. For this reason, patients in long-term uricosuric therapy must be cautioned about the concurrent use of drugs containing salicylate. Although the uricosuric action of phenylbutazone is limited, combination of this drug with salicylate results in loss of this property and, in fact, may cause hyperuricemia.

## Disease States

The arthritis of gout occurs mainly in individuals who have maintained an elevated level of urate for prolonged periods of time. In the past, patients were classified into those who had primary or sec-

ondary gout depending upon whether or not the gout was associated with another disease causing hyperuricemia. This classification is revised in Table 2 by grouping causes of hyperuricemia according to the step in urate metabolism at which the defect is produced.

*Hyperuricemia Due to Increased De Novo Synthesis of Urate*—Some patients with "classical" primary gout belong in this category. These subjects have an increased rate of urate synthesis and usually excrete larger quantities of urates than normal persons. The abnormally high synthesis of urates is due to an overactive "shunt" pathway.

Some recent studies have shown us that a small percentage of adults with classical gout and children with a rare metabolic disorder lack an enzyme, hypoxanthine-guanine phosphoribosyltransferase, which reutilizes hypoxanthine and other purines. The salvage of such purines and their return into active nucleotide pathways permits them to act as negative feedback inhibitors of *de novo* purine synthesis. This is the first demonstration of an inherited biochemical lesion in gout; in the future, other enzymatic defects may be uncovered to account for other cases of increased synthesis.

*Hyperuricemia Due to a Renal Mechanism*—Other patients with classical primary gout seem to have a normal rate of uric acid synthesis as determined by precursor incorporation studies. Their uric acid excretion is within or below normal limits and their clearance ratio of urate to insulin is slightly lower than in nongouty subjects. This lowered renal clearance of urate persists even when serum urate levels are normalized by allopurinol. The precise mechanism for this renal defect has not been established yet. However, there is no evidence of any other impairment of renal function in these patients. It should be mentioned here that the hyperuricemia of classical gout is almost certainly not due to dietary factors. Although a purine-free diet reduces serum urate levels somewhat, it does not fully correct the hyperuricemia.

*Hyperuricemia Due to Increased Nucleic Acid Synthesis and Breakdown*—A high rate of urate synthesis from nucleotides derived from an overactive nucleic acid catabolism is responsible for hyperuricemia in this group of patients. The association of hyperuricemia with lymphomas, leukemias, Hodgkin's disease, multiple myeloma, Waldenstrom's macroglobulinemia, and polycythemia vera is well known. Chemotherapeutic agents often used in these conditions may aggravate the already existing hyperuricemia by destroying cells. The sudden rise of serum urate produced in this manner may cause precipitation of urates in the kidneys and ureters.

Some diseases with a more favorable prognosis are also characterized by high nucleic acid turnover; psoriasis with extensive skin involvement, pernicious anemia treated by vitamin $B_{12}$ or liver extract, and occasionally thalassemia and some hemolytic anemias.

*Hyperuricemia Due to Organic Acid Interference with Renal Tubular Secretion of Urate*—Studies by several workers have shown that infusion of lactate, B-hydroxy-butyrate and acetoacetate will induce a prompt hyperuricemia. These substances seem to compete with the tubular secretion of urate, thereby causing its retention. High levels of serum lactate along with high levels of serum urate can be found in toxemia of pregnancy and von Gierke's disease. High levels of B-hydroxy-butyrate and urate are observed in starvation, diabetic acidosis and in subjects consuming diets high in fats. A transient elevation of lactate and urate is also seen after ethanol ingestion and after vigorous physical exercise.

*Hyperuricemia Due to Diffuse Renal Disease*—Generalized decrease of renal function leads to retention of the several end products of nitrogen metabolism, including urates. Hyperuricemia in uremia is well known, no matter what the primary etiology of renal insufficiency might be. This cause of hyperuricemia assumes greater importance nowadays due to increased use of renal dialysis, thus allowing such patients a more extended period of urate retention.

*Hyperuricemia Due to Unknown Causes or a Combination of Several Above Factors*—Conditions such as primary and renal hypertension, ischemic heart disease, and peripheral arteriosclerosis are associated in a number of instances with hyperuricemia. In a large study of patients with primary and renal hypertension, hyperuricemia was found in more than 40 percent. In patients with myocardial infarction the incidence of hyperuricemia was above 50 percent. A subtle decrease of renal function with hyper-

TABLE 2.—*Clinical Mechanisms for Hyperuricemia*

| | |
|---|---|
| A. | Increased *de novo* synthesis |
| B. | Renal mechanism, unknown type |
| C. | Increased nucleic acid synthesis and breakdown |
| D. | Organic acid interference with renal tubular secretion of urate |
| E. | Diffuse renal disease |
| F. | Absence of enzyme, hypoxanthine-guanine phosphoribosyltransferase, leads to formation of lesser amounts of nucleotide feedback inhibitors, thereby allowing greater *de novo* urate synthesis. |

lactacidemia from the relatively ischemic tissues may be a contributory factor. A number of diseases are associated with hyperuricemia of unknown etiology. These include hyperuricemia found in sarcoidosis, hypo- and hyperparathyroidism, myxedema, and essential hypercholesterolemia.

## Laboratory Methods

Two general methods are available for the determination of serum urate: a colorimetric and an enzymatic procedure. General agreement between these methods usually exists, although the enzymatic procedure tends to give slightly higher values (of the order of about 0.25 mg) since it does not require precipitation of serum proteins and consequent trapping with loss of urate in the precipitate. The enzymatic method using a highly purified preparation of uricase is specific for urate. Although requiring slightly more time than the colorimetric method, equipment for its use is found in most laboratories. The colorimetric technique is still the most widely used and in almost all cases is an adequate test. There are, however, occasional instances when chromagens in serum, beside urate, will contribute to the color obtained and thus, will falsely elevate the value. Such chromagens include gentistic acid, a breakdown product of salicylate metabolism, methylated xanthines in coffee, tea and cocoa, and homogentistic acid elevated in patients with alkaptonuria. In general, serum analysis is less likely to be distorted by these substances, since they are cleared rapidly into the urine. However, when large doses of salicylates are taken, sufficient gentistic acid may be generated to give a false serum elevation of urate of about 1.0 mg percent higher than might occur. To some degree this laboratory artifact might be cancelled out due to the increased excretion of urate that salicylates promote at high dosages (see above). Urine assays as contrasted to serum assays by colorimetric methods are much more hazardous because of the higher concentration of nonurate chromagens.

## Summary

The level of serum urate is an accurate index of the body's pool of this nitrogenous end product. Recognition of its exact value as has been discussed requires a thorough analysis of the patient and his situation. Careful inquiry concerning drug intake and a knowledge of the norms for the laboratory are essential for interpretation of the results. When it can be concluded that the cause for the altered value lies elsewhere, then the results of the general history and complete physical examination of the patient as well as other pertinent laboratory data may furnish the needed clue to explain the altered serum urate value. Gout may indeed be the underlying abnormality, whether it is primary classical gout or gout secondary to another cause. Nevertheless the physician should reinforce his diagnosis by the demonstration of urate crystals in the synovial fluid of the involved joint or bursa. Additional support for the diagnosis may be obtained from a trial of colchicine.

This cautious approach has definite practical value to the doctor and the patient. In the event that gout can be demonstrated and particularly if tophi exist in the patient, an appropriate drug program directed toward reduction of the serum urate value is definitely indicated. Such a program may indeed be life-long and require daily medication and periodic examination including determination of the serum urate value. Also, patients taking probenecid and sulfinpyrazone must be advised to avoid all salicylates, since the combination of drugs results in urate retention.

In summary, the physician must be aware of the complexities that surround the serum urate value. Some of them have been with us for years but many more have been introduced by the widespread use of drugs. In the areas of accurate diagnosis and of effective treatment, a sure knowledge of the factors that influence serum urate values is essential.

(The figures and references may be seen in the original article.)

# SYSTEMIC MAST CELL DISEASE IN A PATIENT WITH UNUSUAL GASTROINTESTINAL AND PULMONARY ABNORMALITIES*

*MAJ Phillip L. Roberts, MC USA,† MAJ Herbert B. McDonald, MC USA, and LT COL Ralph F. Wells, MC USA, El Paso, Texas,* Amer J Med *45(4):638–642, October 1968.*

A forty-one year old man had urticaria pigmentosa since 1954. Systemic mast cell disease became apparent in 1963 and progressed to involve bone, spleen and lymph nodes. There was roentgenographic evidence of widespread involvement of the gastrointestinal tract and a large retroperitoneal mass thought to represent enlarged lymph nodes. Diffuse nodular interstitial infiltrates were apparent on chest roentgenograms and most likely represent pulmonary mastocytosis.

Urticaria pigmentosa for many years was thought to be a dermatologic abnormality, with manifestations limited to the skin. The first autopsy study in 1949 confirmed previous suspicions of systemic involvement in this disease. Since that time a number of cases of systemic mastocytosis have been reported, together with several excellent reviews. Associated abnormalities have included mast cell leukemia, monocytic leukemia, lymphosarcoma, Waldenström's macroglobulinemia, amyloidosis, bleeding diatheses, myelofibrosis, polycythemia vera and gastrointestinal malabsorption.

Described herein is a patient with progressive mast cell disease and unusual gastrointestinal and pulmonary abnormalities. The patient has myelofibrosis and mast cell infiltration of the skin and reticuloendothelial system including spleen, lymph nodes and bone marrow.

## Case Report

A forty-one year old Caucasian man noted progressive skin lesions since 1954, consisting of red-brown macules and papules involving the face, neck, trunk and extremities. The lesions became confluent over the exposed areas of the neck and upper extremities, with marked thickening of the skin in these areas. There was associated pruritus, especially noticeable after bathing and occasionally associated with generalized flushing. He described intermittent episodes of cramping abdominal pain and diarrhea with two to three loose stools daily. A particularly severe episode of abdominal pain occurred in 1962 following ingestion of a cough preparation containing codeine.

The patient was hospitalized at Walter Reed General Hospital in February 1963 and found to have moderate hepatic and splenic enlargement. Urtication and dermatographia appeared after stroking the skin (Darier's sign). The hematocrit was 41 percent, platelets 150,000 per cu. mm. and the leukocyte count 7,500 per cu. mm. with a differential count of 75 percent segmented neutrophils, 6 percent band forms, 27 percent lymphocytes and 2 percent monocytes. Heparin assay of venous blood revealed no significant amount of circulating heparin; alkaline phosphatase was 13.0 King-Armstrong units. Sternal bone marrow aspirate showed prominent mast cell infiltration.

Skeletal roentgenograms revealed an increase in over-all bone density with small areas of osteosclerosis scattered throughout the skull, cervical spine, ribs and proximal portion of the humerus and femur bilaterally. Chest roentgenogram and barium examination of the esophagus, stomach, duodenum and colon were within normal limits except for osteosclerotic lesions of the ribs. A needle biopsy specimen of the liver revealed mild fatty metamorphosis and rare mast cells in portal areas; a skin biopsy specimen disclosed urticaria pigmentosa. In November 1963 splenectomy was performed. The spleen weighed 990 gm. and revealed marked fibrosis and thickening of the cords. Mast cell infiltration was prominent, being especially marked about the fibrous cords. Three months later the leukocyte count was 17,500 per cu. mm. with a differential count of 51 percent segmented neutrophils, 1 percent band forms, 41 percent lymphocytes and 7 percent monocytes; the platelet count was 454,000 per cu. mm.

The patient was first admitted to the William Beaumont General Hospital in March 1966 because of sore throat, cough and slight fever. Throat and sputum cultures were negative; symptoms subsided rapidly following oral treatment with tetracycline.

* From the Department of Medicine, William Beaumont General Hospital, El Paso, Texas. Requests for reprints should be addressed to Maj. Phillip L. Roberts. Manuscript received November 15, 1967.
† Present address: Department of Medicine, Kirk Army Hospital, Aberdeen Proving Ground, Maryland.

Except for moderate pruritus and episodes of generalized flushing, abdominal pain and diarrhea with occasional vomiting, the patient had done well since the onset of his disease. There was no weight loss, anorexia, bleeding, dyspnea or unusual fatigue; he performed military duty without provisions for limitation of physical activity. His past history was significant in that he had an episode of jaundice in 1946, which lasted two to three weeks, associated with anorexia and abdominal pain. This was thought to be viral hepatitis. The patient does not consume alcohol.

Physical examination revealed hepatomegaly; the liver extended 9 cm. below the costal margin. There was generalized lymphadenopathy involving posterior cervical, supraclavicular, axillary and epitrochlear lymph nodes. The skin demonstrated a well healed splenectomy scar in addition to the lesions of urticaria pigmentosa noted previously. The hematocrit was 43 percent, platelets 350,000 per cu. mm. and the leukocyte count was 30,200 per cu. mm. with a differential count of 47 percent segmented neutrophils, 2 percent band forms, 46 percent lymphocytes, 2 percent monocytes and 3 percent eosinophils. There was no significant change in these values over the subsequent eight month follow-up period. During the initial febrile episode, serum bilirubin was 2.5 mg. percent, with 1.5 mg. percent direct reacting fraction. This returned to normal during the ensuing two weeks. Serum glutamic oxalacetic transaminase was 10 units and bromsulfalein retention 8 percent in forty-five minutes. The alkaline phosphatase level was persistently elevated from 3.4 to 4.4 sigma units (normal up to 2.2 sigma units). Serum calcium was 8.7 mg. percent (normal 8.5 to 10.5 mg. percent); phosphorus 4.1 mg. percent. Serum carotene was 24.1 $\mu$g. percent (normal greater than 40 $\mu$g. percent), serum cholesterol 184 mg. percent. Five hour urinary d-xylose excretion following a 25 gm. oral load was 2.5 gm. Sudan-stained fecal specimens were repeatedly negative for fat. Prothrombin time, partial thromboplastin time, blood urea, creatinine clearance, serum protein electrophoresis and immunodiffusion studies were all within normal limits.

Chest roentgenograms demonstrated increased lung markings consistent with a diffuse bilateral interstitial infiltrative process. Steady state carbon monoxide diffusion, forced vital capacity, air flow rates and functional residual capacity by helium dilution technic were all within normal limits. Arterial blood was normally saturated with oxygen both at rest and during exercise.

Roentgenograms of the upper gastrointestinal tract and small bowel revealed marked accentuation of the gastric mucosal folds. Large filling defects were visible in the duodenum; the duodenal loop was widened, and its ascending limb filled poorly at fluoroscopy. The mucosal pattern suggested a diffuse infiltrative process within the small bowel. A lateral supine film revealed anterior displacement of the stomach and duodenal loop by a large retroperitoneal mass. Inferior venacavagram showed slight displacement of the vena cava anteriorly and to the right in the region of the mass. Skeletal roentgenograms demonstrated marked osteosclerosis with patchy areas of bone resorption.

A needle biopsy specimen of bone from the posterior superior iliac spine revealed fibrosis of the marrow spaces with a marked increase in the number of mast cells. A peroral biopsy specimen of mucosa from the region of the ligament of Treitz revealed no specific pathologic diagnosis. There was a slight increase in lymphocytes, plasma cells and eosinophils within the submucosa. Mast cells were not increased in number. A lymph node biopsy specimen from the axilla showed a moderate increase in fibrous tissue and a marked increase in mast cells. The latter were most prominent in the capsule and fibrous areas of the node. A skin biopsy specimen showed urticaria pigmentosa; the dermis was diffusely infiltrated with mast cells.

## Comments

Systemic mastocytosis, due to an abnormal proliferation of mast cells, may involve virtually all organ systems. Although urticaria pigmentosa usually antedates clinical evidence of systemic disease, several cases of advanced mast cell disease without skin involvement have been described. The similarity to myeloproliferative syndromes has been noted, and the association of systemic mastocytosis with myelofibrosis, myeloid metaplasia and polycythemia vera is well documented.

The role of the mast cell in human physiology remains uncertain. Histamine and heparin are known to be present in mast cells; the evidence for serotonin is less clear. Many symptoms of mast cell disease may be attributable to the release of histamine. Pruritus, urtication, flushing, nausea, vomiting, abdominal pain, diarrhea and hypotension can all be produced by the administration of histamine. His-

taminuria has been demonstrated in most patients studied for urinary histamine; in some a positive correlation with symptoms has also been found.

Vilanova et al. presented inconclusive evidence suggesting a circulating inhibitor of coagulation in a nine-month old child with mastocytosis and bleeding from the site of a skin biopsy. The inhibition was neutralized with protamine. Berlin demonstrated an inhibitor of coagulation in blood obtained from skin lesions; no inhibition was detected in peripheral blood. The latter patient was a seventy-one year old man with bleeding from involved areas of skin. The striking association of mast cell proliferation and fibrosis has been noted frequently and is thought to be related to the effect of heparin released from mast cells.

Roentgenographic evidence of gastrointestinal abnormalities in mastocytosis is usually limited to manifestations of ulcer disease. It is interesting in this regard that gastric secretion of hydrochloric acid is most often normal or reduced. In 1962 Janower described the only previous patient with roentgenographic evidence of widespread gastrointestinal mastocytosis; this was confirmed histologically following laparotomy. In our case roentgenograms revealed similar abnormalities and suggested an infiltrative process involving the stomach and small bowel. Although a mucosal biopsy specimen from the small intestine did not reveal an increased number of mast cells, this does not exclude gastrointestinal mastocytosis; on roentgenologic grounds it is considered likely. Usually gastrointestinal symptoms are related to peptic ulcer disease or histamine release. Two well documented cases of gastrointestinal malabsorption with steatorrhea have also been reported. In one, jejunal and ileal biopsy specimens obtained at laparotomy showed partial villous atrophy; increased numbers of mast cells were not seen. Steatorrhea was not demonstrated in our patient; the low serum carotene level and the abnormal d-xylose absorption test may reflect a mild degree of malabsorption, although there had been no weight loss.

The large retroperitoneal mass most likely represents enlarged lymph nodes with infiltration by mast cells, but since exploratory surgery was thought not to be therapeutically indicated histologic proof of this is lacking. However, there is no evidence of lymphoma, leukemia, amyloidosis or infectious disease; the enlarged axillary node revealed mast cell proliferation and fibrosis; coagulation studies were within normal limits.

The interstitial pulmonary infiltration in our patient was not accompained by symptoms of cardiopulmonary disease; pulmonary function studies were normal. Mutter et al. described a patient in whom extensive peribronchial and alveolar infiltration with mast cells was found at autopsy. A small cavitary nodule noted antemortem had closed spontaneously. Szweda et al. described one patient with increased pulmonary vascularity and fibrotic densities scattered throughout both lung fields which were thought possibly to be due to mast cell infiltration. Their patient also had mitral stenosis.

Systemic mastocytosis is a chronic and progressive disease. Spontaneous regression has never been documented. This is in contrast to the frequent disappearance of urticaria pigmentosa in early childhood. Mutter et al. reviewed the literature up to 1963 and found twenty-nine patients with systemic mastocytosis; eleven had died, with an average survival of 2.6 years after the onset of symptoms. The remaining eighteen, who were living at the time of the reports, were symptomatic for an average of 4.2 years; three had had symptoms for more than ten years, and the longest survivor had been symptomatic for twelve years.

No satisfactory treatment is available. Antihistamine and antiserotonin drugs have been used with variable symptomatic relief. Corticosteroids, polymyxin B, nitrogen mustard, vincristine and radiation therapy have been tried without dramatic improvement. The use of radiation therapy and cytotoxic agents has been associated with symptoms of increased histamine release; opium derivatives and salicylates may also intensify these symptoms.

(The figures and references may be seen in the original article.)

# MEDICAL ABSTRACTS

## BLUNT ABDOMINAL TRAUMA

*F. C. DiVincenti, MD, et. al., J Trauma 8(6):1004-1013, Nov 1968.*

The records were reviewed of 518 consecutive patients with blunt abdominal trauma seen during the 15-year period from 1951 through 1966. The records were evaluated as to cause, effect and mortality in each type of injury.

The overall mortality was 23 percent, and among patients operated on it was 14 percent.

Associated extra-abdominal injuries were the most significant factor in increasing mortality.

Rupture of the spleen was the most common visceral injury, and was associated with an operative mortality of 14 percent.

Liver injuries were associated with the overall high mortality of 49 percent. The operative mortality in rupture of the liver was 26 percent.

Rupture of the urinary bladder was seen in 36 patients. Other hollow viscera were ruptured in 52 patients with an overall mortality of 15 percent, and operative mortality of 10 percent.

Percutaneous four-quadrant aspiration of the peritoneal cavity proved to be a most valuable and accurate diagnostic procedure.

Emphasis was placed on the importance of a carefully prearranged plan for the emergency care, diagnosis and management of the injured patient and on the value of a well-trained team for the care of the patient with blunt abdominal trauma.

## COAGULATION DISORDERS IN COMBAT CASUALTIES

*CAPT R. L. Simmons, MC USAR, et. al., Ann Surg 169(4): 455-482, Apr 1969.*

Part I—Acute Changes after Wounding

A number of coagulation parameters were studied in acutely wounded combat casualties on arrival at the hospital and prior to administration of any intravenous therapy.

Fibrinolysin levels were higher than normal but platelet counts and fibrinogen levels were not consistently abnormal.

The prothrombin (PT) and partial thromboplastin times (PTT) could be statistically correlated with the degree of hypotension, acidosis, and lactatemia. Mildly to moderately wounded patients had normal or shortened PT and PTT. Severely wounded patients in shock had normal or prolonged PT and PTT.

The findings are consistent with experimental observations that trauma and shock produce an initial phase of hypercoagulability followed by a return to normal and a phase of hypocoagulability. The hypocoagulable phase seems best explained by the onset of disseminated intravascular coagulation precipitated by hemolysis, the release of tissue thromboplastin, acidosis, and the state of hypoperfusion seen in patients in hypovolemic and traumatic shock.

The severity of the coagulation defect in these young men is mild. The effect of similar qualitative changes in more debilitated civilian casualties is discussed.

Part II—Effects of Massive Transfusion

Transfusion of combat casualties is accompained by dilutional coagulation defects compatible with levels of coagulation factors in stored bank blood. Platelet levels fell rapidly during transfusion to about 100,000/mm. The prothrombin times, partial thromboplastin times, and fibrinogen levels were less severely affected.

Significant operative bleeding was not encountered in conjunction with these mild dilutional coagulation changes.

The administration of stored bank blood to casualties who have developed coagulation defects secondary to shock results in a partial return of coagulation factors toward normal. Pre-existing coagulation defects were not aggravated by thromboplastic substances in bank blood.

Transfusion with stored bank blood may mask the appearance of endogenous coagulation disorders which develop in patients in prolonged shock.

The use of fresh whole blood will partially counteract the dilutional effect on coagulation parameters but is rarely necessary in young, previously healthy men. In the presence of coagulation defects associated with presumed disseminated intravascular coagulation, fresh whole blood was not associated with any permanent improvement in coagulation parameters

Part III—Post-Resuscitative Changes

Coagulation studies were performed as often as three times daily on 120 combat casualties during early convalescence.

The prothrombin times and partial thromboplastin times of almost all patients were normal within the first 24 hours after resuscitative operations. There-

after, abnormalities occurred in either or both parameters in 57 patients. Coagulation abnormalities could be correlated with the presence of shock on admission to the hospital, transfusion of large quantities of blood, and the presence of abnormalities in clotting parameters prior to operation.

The degree of prolongation of PT or PTT was much greater than that seen either at the time of admission or during transfusion.

In 24 patients a pattern of recurring PT or PTT prolongations appeared in the postoperative period with intervening periods in which these parameters were normal. The presence of four or more of these peaks could be correlated with the appearance of life-threatening complications. All patients who died had abnormalities at some time prior to death. Bleeding episodes which required reoperation, however, were not associated with coagulation abnormalities.

Fibrinogen levels were greater than normal in almost all patients. This pattern of recovery was delayed in patients who had been in shock on admission, or who developed prolongations of PT or PTT during convalescence.

Platelet counts returned to normal over the first week in almost all patients. Recovery was delayed in those who had been in shock on admission, who had received large quantities of blood, or who developed prolongations of PT or PTT during convalescence.

Fibrinolysin values returned toward normal but remained elevated in most patients during the first convalescent week. The values were significantly higher if prolongation of PT and PTT were present during this period but no correlation could be made with the degree of shock on admission.

The coincidence of abnormalities of PT and PTT with thrombocytopenia and fibrinolysis, and a relative deficiency of fibrinogen in most seriously wounded patients is consistent with the idea that nonlethal episodes of disseminated intravascular coagulation occur during recovery from severe trauma and shock.

## JAUNDICE IN ACUTE APPENDICITIS

*D. F. Miller and R. W. Irvine, Lancet I(7590): 320-323, Feb 15, 1969.*

In a series of 120 consecutive cases of acute appendicitis jaundice ensued in 9 (7.5%) after appendicectomy. The jaundice was commonly associated with severe *E. coli* infection, and may be a hepatoxic effect of this organism. The jaundice was not severe and resolved quite quickly. It tended to occur in the more severely infected cases, but did not seem to increase the morbidity significantly. The recognition of this form of jaundice is important, in order to avoid wrongly suspecting gallbladder disease, infectious hepatitis, or the effects of anaesthetic agents or drugs.

## RECOGNITION AND TREATMENT OF MELANOMA

*Robert J. Booher, MD, Surg Clin N Amer 49(2): 389-405, Apr 1969.*

In a series of 267 patients with melanoma treated at Memorial Hospital prior to 1931, a 5-year survival rate of 12 percent was reported in 1936 by Adair. Later Pack, Gerber, and Scharnagle reported a similar 10-year cure rate in patients treated before 1940, at which time a radical surgical approach became routine. In this 1952 report of 1,190 patients, 40.5 percent of patients who had no metastases to nodes remained free of tumor for more than 5 years, compared to only 14.1 percent of those with lymph node metastases.

Eleven years later, McNeer and Das Gupta reviewed a total of 804 patients with histologically verified melanoma of the trunk and extremities, observed between 1935 and 1955; of the total, 779 were determinate cases. At that time, primary melanoma was found to offer a 5-year survival rate of 71.5 percent and a 10-year survival rate of 62 percent, while stage II melanoma (tumors with regional node metastases) had a 12 percent cure rate at 10 years. It is of course apparent that staging the tumors affects the cure rate remarkably, but the fact that 62 percent of those patients whose melanoma was still localized to the primary site were cured in 10 years stands in opposition to the observation made 11 years earlier that although melanoma is the most accessible of all major forms of cancer, it has the unwelcome distinction of the lowest curability. Undoubtedly surgeons have contributed greatly to this remarkable improvement in the outlook for patients with melanoma, but of equal importance is the earlier detection of this tumor. Allen observed that the histologic differentiation of pigmented lesions by biopsy occurs much earlier today than 30 years ago.

## PHOTOSENSITIVE DERMATITIS FROM SOAPS

*A. E. Ison, MD, and CAPT J. B. Tucker, MC USAF, New Eng J Med 278(2): 81-84, Jan 11, 1968.*

Antibacterial soaps containing halogenated salicyl-

anilides cause photosensitive skin eruptions that can be reproduced by a simplified photopatch testing technic. Twelve patients with photosensitive reactions due to soaps had positive tests to either dibromosalicylanilide or tribromosalicylanilide, or a soap solution containing these substances, but tests were negative if soap solutions free of halogenated salicylanilides were used. Of 21 patients with other dermatologic diseases only one had a positive test to halogenated salicylanilides. Comparative photopatch tests in sensitive patients with a series of halogenated salicylanilides in current use showed no significant difference in the number of positive reactions to the several agents tested.

## DEVELOPMENT OF THE PRESENT CONCEPT OF HEMOPHILIA

*H. E. Hynes, MB B.CH, et. al., Mayo Clin Proc 44(3): 193-206, Mar 1969.*

Hemophilia was not established as a distinct clinical entity before the 19th century. However, it is known that cases of hemophilia occurred before that time. References in *Tractat Jabomoth* of the Talmud to the occurrence of fatal bleeding after circumcision in the sons of several sisters suggest that the disease was known to the ancient Jews. Albucasis, a Moorish surgeon in the 10th century, described a severe hemorrhagic diathesis occurring in males.

The first case of hemophilia recorded in the medical literature was published in 1793 in *Medicinische Empheremiden* by an anonymous author, probably G. W. Cornsbruch (according to Bulloch and Fildes). However, the hemophilic family described in 1803 by Otto, a Philadelphia physician, was the first to attract wide attention, and soon afterward other reports appeared in the literature in the United States and Europe.

Classic hemophilia is a sex-linked hereditary disease characterized by a lifelong tendency of the afflicted person to bleed excessively after trauma or even spontaneously. The hemostatic defect is due to inefficient coagulation of blood, the basic cause of which is deficiency or inactivity of a plasma coagulation factor, factor VIII. Although it is uncertain whether there is a deficiency of factor or overproduction of an inhibitor in hemophilia, the important fact from the clinical standpoint is that transfusion of normal plasma or certain plasma fractions is effective therapy.

## SURGICAL TREATMENT OF AMEBIASIS

*William P. Grigsby, MD, Surg Gynec Obstet 128 (3): 609-627, Mar 1969.*

Amebiasis is an infection in man caused by Entamoeba histolytica. This pathogenic protozoan localizes primarily in the colon, from where it may disseminate to the liver, lungs, and other organs. Infection is acquired by the ingestion of viable Entamoeba histolytica cysts contained in fecally contaminated food or water. Amebiasis is cosmopolitan and is endemic in most tropical countries. In the United States the incidence of amebic infection is calculated to affect less than four percent of the population and clinical amebic disease is not common.

The clinical severity of amebiasis varies from asymptomatic to fulminant degrees. In the majority of patients only cysts are passed in the stools and clinical symptoms are not present. Diarrhea and dysentery, the most common clinical manifestations of amebiasis, occur in about five percent of infected persons. Intestinal amebiasis may be complicated by such conditions as perforation, peritonitis, and liver abscess. Amebiasis can usually be treated successfully with drugs; however, complications which require surgical treatment develop in an estimated 0.5 percent of dysenteric patients. While these complications constitute a small fraction of the total amebic morbidity, their life-threatening potential lends them special importance. The purpose of this article is to outline from a clinical viewpoint the pathologic factors, diagnosis, and management of surgically treated amebic lesions.

# RESEARCH SECTION

## LIST OF RECENT PUBLICATIONS FROM RESEARCH LABORATORIES

The following papers have been completed by research activities under the direction of the Bureau of Medicine and Surgery.

*Naval Aerospace Medical Institute, Pensacola, Fla.:*

"Dynamic Response of the Head and Neck of the Living Human to —$G_X$ Impact Acceleration" by C. Ewing, D. J. Thomas, G. W. Beeler, Jr., L. M. Patrick, and D. B. Gillis. 12th Stapp Car Crash Conference, 1968.

"Egocentric Visual Localization in Normals and Partially Blind During Exposure to Centripetal Force" by Brant Clark and Ashton Graybiel. *American Journal of Psychology,* Vol. LXXXI, Sept 1968.

"Effect of Drugs on Ocular Counterrolling" by Earl F. Miller and Ashton Graybiel. *Clinical Pharmacology and Therapeutics,* Vol. 10, No. 1, Jan-Feb 1969.

"Prevention of Overt Motion Sickness by Incremental Exposure to Otherwise Highly Stressful Coriolis Accelerations" by Ashton Graybiel, F. R. Deane, and J. K. Colehour. *Aerospace Medicine,* Vol. 40, No. 2, February 1969.

"Structural Elements in the Concept of Motion Sickness" by Ashton Graybiel. *Aerospace Medicine,* Vol. 40, No. 4, April 1969.

"Study of Blood pH, Serum Potassium Concentration, and Stress in the Squirrel Monkey (*Saimiri sciureus*)," by T. E. Wheeler and A. E. New. NAMI-1041, December 1968.

"Motion Sickness Precipitated in the Weightlessness Phase of Parabolic Flight by Coriolis Accelerations" by Ashton Graybiel, Robert S. Kennedy, and Robert S. Kellogg. NAMI-NASA Project. NAMI-1061, February 1969.

"Motion Sickness Susceptibility Under Weightless and Hypergravity Conditions Generated by Parabolic Flight" by E. F. Miller II, Ashton Graybiel, R. S. Kellogg, and R. D. O'Donnell. NAMI-NASA Project. NAMI-1057, January 1969.

"Nuclear Emulsion Measurements of the Astronauts; Radiation Exposure on Appollo VII" by Hermann J. Schaefer and Jeremiah J. Sullivan. NAMI-NASA Project. NAMI-1060, February 1969.

"Somatic Chromosomes of the Mongolian Gerbil (*Meriones unguiculatus*)" by Steven P. Pakes. NAMI-U.S. Army Aeromedical Research Laboratory Project Serial No. 69-4. NAMI-1056, January 3, 1969.

*Naval Dental School, Bethesda, Md.:*

"Effect on Airborne Bacteria of Extraneous Particulate Matter or Air Filtration" by W. B. Shreve, G. B. Pelleu, Jr., and L. W. Wachtel. NDS-TR-007, January 7, 1969.

"Reduction of Microbial Concentration in Air of Dental Operating Rooms by Hepa Filtration" by G. B. Pelleu, Jr., and L. W. Wachtel. NDS-TR-007, January 7, 1969.

"Reduction of Microbial Concentration in Air of Dental Operating Rooms by Hepa Filtration" by G. B. Pelleu, Jr., W. B. Shreve, and L. W. Wachtel. NDS-TR-008, January 21, 1969.

*Naval Hospital, Philadelphia, Pa.:*

"Combat Fatigue Versus Pseudo-Combat Fatigue in Vietnam" by R. E. Strange. *Military Medicine,* Vol. 133, No. 10, October 1968.

"Management of a Thermal Burn with Amputation and Reconstruction of the Penis" by R. Julian, M. H. Klein, and H. Hubbard. *Journal of Urology,* Vol. 101, April 1969.

"Pulmonary Function Before and After Left Lung Autotransplantation" by A. A. Birch, Jr., W. L. Secrist, M. K. Becker, and M. J. Trummer. *Archives of Surgery,* Vol. 97, 1968.

*Naval Medical Field Research Laboratory, Camp Lejeune, N. C.:*

"Effect of Protein Dietary Supplementation on the Physical Performance of Marine Corps Officer Candidates" by P. J. Rasch, J. W. Hamby, and H. J. Burns, Jr. NMFRL Report Vol. XIX, No. 6, March 1969.

"Serum Uric Acid Level and Military Motivation" by P. J. Rasch, J. S. Bird, J. W. Hamby, and H. J. Burns, Jr. *Military Medicine,* Vol. 134 No. 2, February 1969.

*Naval Medical Neuropsychiatric Research Unit, San Diego, Calif.:*

"Correlational Analysis of the Relationships Between Personality and Perceptual Variables and Discriminant GSR Conditioning" by George A. Glum. *Journal of Clinical Psychology,* Vol. XXIV, No. 1, January 1969.

*Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.:*

"Aryl Ester Infusion and Evoked Responses from the Soleus-Gastrocnemius Tissue Complex in the Cat" by S. L. Friess, R. C. Durant, H. L. Martin, W. V. Hudak, and H. Weems. *Toxicology and Applied Pharmacology.* Vol. 14, 1969.

"Attempts to Transmit Infectious Mononucleosis to Rhesus Monkeys and Marmosets and to Isolate Herpes-Like Virus" by P. Gerber, J. W. Branch, and E. N. Rosenblum. *Proceedings of the Society for Experimental Biology and Medicine,* Vol. 130, 1969.

# DENTAL SECTION

## FIFTY-SEVENTH ANNIVERSARY OF THE NAVAL DENTAL CORPS

It is a pleasure to extend my personal greetings to the officers of the Naval Dental Corps in commemoration of the Corps' 57th Anniversary on 22 August. As a component of the Medical Department, you have continued to render vital support to the medical team in caring for personnel in the combat theater of Southeast Asia. Your contribution to the health care of all members of the Navy and Marine Corps has been outstanding.

Congratulations and best wishes for the continued success of your many professional programs.

G. M. DAVIS
Vice Admiral, MC, USN
Surgeon General

To all Naval Dental Officers, I extend hearty best wishes on the occasion of the Fifty-seventh Anniversary of the Naval Dental Corps on 22 August 1969.

It is an appropriate time to reflect with gratitude and pride, the rich legacy bestowed on us by our predecessors. This heritage, so generously given, serves as an inspiration and as a challenge to maintain our leadership in the profession of military dentistry.

In these troubled times, special mention must be made for the dedicated dental personnel in Southeast Asia, both ashore and afloat, who are distinguishing themselves in the service of their country. Their accomplishments are magnificent and they display an exceptionally high state of morale.

All of us associated with dentistry in the Navy, look with renewed dedication and confidence to a brighter tomorrow for ourselves, our Navy and our Nation.

I salute each of you and consider it an honor to represent you in our efforts to provide the highest quality of dental care to all personnel in our wonderful Navy and Marine Corps.

Happy Birthday!

E. C. RAFFETTO
Rear Admiral, DC, USN
Assistant Chief of the Bureau of Medicine and Surgery (Dentistry) and
Chief, Dental Division

# PERSONNEL AND PROFESSIONAL NOTES

## CAPTAIN ARTHUR SELECTED FOR PROMOTION TO REAR ADMIRAL

CAPT John P. Arthur, DC USN, was selected for promotion to the rank of Rear Admiral on 16 June 1969.

CAPT Arthur received his D.M.D. degree from the North Pacific Dental College, Portland, Oregon in 1940 and entered private practice in Albany, Oregon, following graduation.

Upon being commissioned a LT(jg) in the Naval Dental Corps in 1941, he was assigned to the Second Marine Division. He also served on the USS INDIANA (BB–58) and in Korea with the First Marine Division during the Korean conflict. As a result of his service in Korea, he became entitled to wear the Korean Service Medal with five engagement stars and the Marine Corps Insignia, the Presidential Unit Citation with two stars, the South Korean Presidential Unit Citation with an Oak Leaf Cluster and the United Nations Medal.

CAPT Arthur is presently serving as Assistant to the Chief of the Dental Division, Bureau of Medicine and Surgery. Prior to this assignment he served as Executive Officer, Naval Dental Clinic, Norfolk, Virginia.

## MAXILLOFACIAL PROSTHETICS IN NAVAL FACILITIES

The specialty of maxillofacial prosthetics had its beginning in the Navy during World War II when dental officers at the Naval Dental School developed the acrylic eye. Due to the shortage of glass eyes, ophthalmologists had sought the knowledge and skills of the dental officer in a search for an adequate plastic ocular prosthesis. Today, the acrylic eye is used universally.

At the same time, the need for other maxillofacial devices became apparent, and dental officers engaged in studies that grew into a much needed specialty. Since World War II, maxillofacial prosthetic specialists in the Naval Dental Corps have been trained at the Naval Dental School and civilian universities, and have been practicing at the Dental School and at the Naval Hospital in San Diego. Other hospitals have had this service from time to time, depending on the training and experience of the dental officers assigned.

Additional capabilities have recently been developed due to the increased demand for maxillofacial prosthetic treatment for Vietnam patients. In addition to the services at the Naval Dental School and at the Naval Hospital, San Diego, the naval hospitals in Oakland, Calif., and Great Lakes, Ill., are providing all types of maxillofacial prosthetic treatment. Dental officers at the four facilities have completed a residency in maxillofacial prosthetics in addition to their 2 years of graduate level training in prosthodontics, and each facility has an experienced prosthetic dental technician who has been trained in maxillofacial prosthetic techniques.

Intra-oral, extra-oral, and implant prostheses can be fabricated in the four facilities. The intra-oral structures usually are replacements for portions of the maxilla or mandible. The extra-oral appliances include eyes, ears, noses, portions of the cheek, and, sometimes, combinations of anatomic structures; for it is not uncommon for a victim of cancer to lose not only the maxilla but also the orbital contents or the nose. Typical implants are cranioplates, cosmetic augmentation implants, mandibular replacements, and other devices designed to be buried into the tissue.

While only a few special materials and equipment are needed to fabricate the appliances, quiet, pleasant treatment spaces, separated from laboratories and offices, help a great deal in the patient's psychological rehabilitation. For this reason, the maxillofacial clinic at the Naval Dental School was completely renovated in 1967, and spaces at the Naval Hospital in Oakland are now being renovated.

More prosthodontists and technicians will be trained, in long courses, in this highly specialized area to increase the capability of other naval hospitals. For the first time, a 1-week continuing education course in maxillofacial prosthetics, limited to prosthodontists, will be offered at the Naval Dental School, in 1970.

Eventually every service in a hospital may find the need for a maxillofacial prosthetic appliance. It may be for a custom-designed implant, an ocular prosthesis, a mouth stick for a paraplegic, or a strut to be used in conjunction with surgery. While war injuries created the initial need for maxillofacial prosthetics, the service is invaluable in peacetime when the need for replacement of missing or defective parts results from surgical intervention, trauma, disease, or developmental anomaly.

If all personnel who treat hospital patients, will keep in mind the potential of the maxillofacial prosthetic service, very likely they will find that the appliances required can be provided by this service.

## GRADUATION AT NAVAL DENTAL SCHOOL

On June 20, the Naval Dental School held graduation ceremonies for 44 Dental Corps officers who completed graduate-level courses in general dentistry and various dental specialties.

Mr. Charles O. Bennett, Jr., Governor Elect of District 762, Rotary International, gave the graduation address. After speaking of the present breakdown in morality, law, and order, he told the graduates that the youth of our Nation needs the inspiration to bring about a spiritual revolution and that, because of their professional contacts with the young servicemen, they are in a unique position to impart such inspiration through their understanding, maturity, and example.

Three awards were made for outstanding achievement in the first year graduate level courses. CDR Meredith S. Burch received the Commanding Officer's Award for General Excellence; LCDR George A. Short, the Commanding Officer's Award for Excellence in Operative Dentistry; and LCDR Charles A. Brown, the Naval Dental School Award for Achievement in Research Methods. LCDR Short has been assigned to the staff of the Naval Dental School, while CDR Burch will attend a second year graduate level course in oral surgery at the Naval Hospital, Philadelphia, and LCDR Brown will attend a similar course at the Naval Hospital, St. Albans.

## NAVAL DENTAL CORPS CONTINUING EDUCATION PROGRAM

The Continuing Education Courses presented at the Naval Dental School, and those sponsored by Commandant, Eleventh Naval District, Naval Dental Center, San Diego, California, are scheduled as follows during Fiscal Year 1970:

*Naval Dental School, Bethesda, Maryland*

| *Courses* | *Dates* |
|---|---|
| Oral Surgery | 5–9 January 1970 |
| Oral Pathology | 12–17 January 1970 |
| Oral Roentgenology | 19–23 January 1970 |
| Fixed Partial Dentures | 9–13 February 1970 |
| Removable Partial Dentures | 16–20 February 1970 |
| Preventive Dentistry | 23–27 March 1970 |
| Operative Dentistry | 30 Mar–3 Apr 1970 |
| Occlusion | 13–17 April 1970 |
| Complete Dentures | 20–24 April 1970 |
| Maxillofacial Prosthetics* | 27 Apr–1 May 1970 |
| Periodontics | 4–8 May 1970 |
| Endodontics | 11–15 May 1970 |

Quotas have been assigned to District and Staff dental officers for career dental officers, and Reserve dental officers on active duty on a space available basis. District Commandants have likewise been assigned quotas for inactive Naval Reserve Dental Officers (Ready Reserve).

For courses at the Naval Dental School, applications from career officers and Reserve officers on active duty are to be submitted via the chain of command and in accordance with current directives to the Chief, Bureau of Medicine and Surgery (Code 6), Navy Department, Washington, D. C. 20390, in the format shown in MANMED article 6-130. Naval Reserve officers (Ready Reserve) will apply to their District Commandant via the Director of Naval Reserve Activities or the District Dental Officer.

*Naval Dental Center, San Diego, California*

| *Courses* | *Dates* |
|---|---|
| Removable Partial Design | 17–19 September 1969 |
| Fixed Partial Dentures | 15–17 October 1969 |
| Operative Dentistry | 3–7 November 1969 |
| Occlusion | 10–12 December 1969 |
| Endodontics | 7–9 January 1970 |
| Complete Dentures | 11–13 February 1970 |
| Oral Surgery | 9–13 March 1970 |
| Preventive Dentistry | 8–10 April 1970 |
| Periodontics (Basic) | 6–8 May 1970 |

For courses at the Naval Dental Center, San Diego, career dental officers and Reserve dental officers on active duty should submit their applications via the chain of command and in accordance with current directives to the Commandant, Eleventh Naval District (Code 37), San Diego, California 92130, in the format contained in MANMED article 6-130. Naval Reserve officers (Ready Reserve) will apply to the Commandant, Eleventh Naval District via their appropriate District Commandants.

Application should be submitted so as to be received at least one month prior to the convening date of the course. Officers will be notified regarding the action taken on their requests. Those approved will be nominated for TAD, authorization orders, or active duty for training as appropriate.

*Limited to Prosthodontists

### DENTAL DEPARTMENT-USS FULTON LETTER OF COMMENDATION

The Officers and crew of the Dental Department, USS FULTON (AS11) received letters of commendation from the Commanding Officer for the extensive dental treatment provided to 87 children from two orphanages in San Juan, Puerto Rico, during SPRINGBOARD 1969. The commendation read in part, "You unselfishly and enthusiastically gave of your shore leave to be of service to others. I note with pleasure the thank you and well done received by this command from Commander Caribbean Sea Frontier, for this generous action in support of the People to People Program. Your performance was a direct contribution to the good image of the Navy and FULTON in Puerto Rico. Your willingness to be of service to others, even at the expense of inconvenience to yourself, exemplifies the spirit of cooperation and traits of leadership which the Navy in general and this command in particular may be justly proud."

The personnel receiving the commendations were: CDR W. R. Cotton, LT B. M. Elliott, LT H. C. Giles, Jr., DT2 K. C. Craig, DT2 D. C. Manger, DT3 J. A. Hollifield, DT3 L. T. Aho, DT3 L. Warchola and Dental Technician striker R. Glynn.

### WAVE DENTAL TECHNICIAN PROMOTED TO MASTER CHIEF PETTY OFFICER

Johnnie L. Davis, an instructor at the Dental Technicians School, is the first WAVE to be promoted to Master Chief Dental Technician. In congratulating Chief Davis upon her advancement, RADM Frank M. Kyes, DC USN, Director, Dental Activities, Eleventh Naval District, and Commanding Officer, Naval Dental Center, San Diego, acknowledged the high esteem her students, past and present, hold for her.

Chief Davis' new assignment is at the Administrative Command, Naval Training Center, Great Lakes, Illinois.

### AWARDS AND DECORATIONS

*Navy Commendation Medal with Combat Device*
CDR M. B. Brenyo, DC USN

*Navy Achievement Medal*
LCDR R. B. Drysdale, DC USN
LCDR J. L. Luhtala, DC USN

*Vietnamese Armed Forces Honor Medal, 1st Class; and Technical Service Medal, 1st Class*
CDR E. P. Klecinic, DC USN

## PROFESSIONAL RELATIONS PROGRAM

### ARMY INSTITUTE OF DENTAL RESEARCH STUDENTS VISIT NAVAL DENTAL SCHOOL

Sixteen students in the Advanced Theory and Science of Dental Practice Course, at the Army Institute of Dental Research, Walter Reed Army Medical Center, recently visited the Naval Dental School. The purpose of the visit was a mutual exchange of ideas on professional development, since the course in which the Army graduate students are enrolled is similar to the Graduate Courses conducted at the Naval Dental School.

### SOUTH AFRICAN NAVY DENTAL OFFICER VISITS NAVAL DENTAL SCHOOL

LT James Burger, a dental officer in the South African Navy, recently visited the Naval Dental School. Doctor Burger, whose father is the South African Defence Forces Attache to the United States, also visited naval facilities in Norfolk, Virginia, and San Diego, California. He is stationed at the S.A.N. Medical Center, Simonstown, Cape, Republic of South Africa.

The curriculums of the various graduate courses were of special interest to Doctor Burger since his country recognizes only two specialties—oral surgery and orthodontics.

## ARTICLES AND ABSTRACTS

### A REVIEW OF AEROBIOLOGY AS APPLIED TO THE PRACTICE OF DENTISTRY

*LCDR Dennis D. Flynn, DC USN.*

An aerosol can be defined as "any system of liquid droplets or solid particles dispersed in air, of fine enough particle size, and consequent low settling velocity, to possess considerable stability as an aerial suspension." Dental aerosols may contain one or any combination of the following components: oro-naso-pharyngeal microorganisms; dust and larger particles from metallic restorations, silicates,

dentin and enamel; bur flukes, debris from cuttlefish and sandpaper discs; free saliva and water; and hemorrhagic elements resulting from soft tissue manipulation.

The monograph consists of (1) a historical review of some theories on airborne microbes and disease transmission, (2) a short review of those structures of the human respiratory tract which are important in particle capture, (3) the nature and fate of inhaled particles as they enter and traverse the respiratory system, (4) a literature review of dental aerosols plus a brief discussion of what is known of the possible pulmonary sequelae of inhaling proteinaceous substances and mercury vapors, and (5) a review of methods which have been tried and tested for air sterilization, of methods available to dentists today, and a projection of some methods for future consideration.

Within the Appendix can be found three backlighted photographs of mechanically-generated aerosols, two of which were taken during actual clinical procedures. Also shown are pictures of one of the most popular air sampling devices and a Stanford Research Institute chart depicting the approximate sizes of many organic and inorganic particles which may be inhaled into the human respiratory system.

Many questions have been raised as a result of such a literature review: Do dentists build up immunities to some diseases by virtue of constant close proximity to patients; are we, indeed, carriers of certain diseases; do delicate and metallic particles lodge in the alveolar spaces of our lungs and can mercury droplets penetrate to these regions; why do dentists have a higher mean age of death from pulmonary diseases than the average U.S. male over 24 years of age?

Two conclusions are put forth: (1) until more is known about the dentist and his personnel as potential carriers of disease and the immunology of dental practice, each dentist should afford himself and his patients with the maximum protection obtainable, and (2) only with an increase in the vigor of dental aerobiological research will investigators be able adequately to determine the human response to clincial dental practice.

(Copies of the monograph can be obtained by addressing requests to: Commanding Officer, Naval Medical Research Unit #1, Bldg. T-19, Berkeley, California 94720.)

(Abstracted by LCDR Dennis D. Flynn, DC USN.)

The opinions or assertions contained herein are those of the author and are not to be construed as official or as reflecting the view of the Navy Department or the Naval Service at large.

## REDUCTION OF MICROBIAL CONCENTRATION IN AIR OF DENTAL OPERATORY ROOMS BY HEPA FILTRATION

*G. B. Pelleu, Jr., W. B. Shreve, and L. W. Wachtel.*

Microbial aerosols are known to be created and disseminated in dental operating rooms (DOR's) in quantities sufficient to raise the possibility of cross infection. The purpose of this study was to evaluate the effectiveness of high efficiency particulate air (HEPA) filters in reducing the concentration of airborne microorganisms. Tests were made in DOR's of 1600-, 1800-, and 3240-ft$^3$ capacity with an 800-cfm HEPA filter unit. Concentrations of microorganisms were measured 4 times daily at approximately 2- to 3-hour intervals. Samples were taken in each DOR with 1-hour Reyniers air samplers drawing 1 cfm for 2 weeks without air filtration and then for 2 weeks with air filtration. In a DOR used for routine scaling with an ultrasonic instrument, the mean microbial air count of 21 viable particles (VP)/ft$^3$ without air filtration was reduced 90 percent when the air was filtered. In this DOR, peak recoveries of 185 VP/ft$^3$ without air filtration were reduced 84 percent when the air was filtered. Bacteria recovered during peak periods were predominantly alpha-hemolytic streptococci of the viridans group. In two DOR's used only for routine operative dentistry, microbial air counts were lower, with mean values of 3-8 VP/ft$^3$ and peak values of 8-26 VP/ft$^3$ without air filtration. These concentrations were reduced 65 percent when the air was filtered. It was concluded that under normal working conditions an 800-cfm HEPA filter unit is effective in reducing the concentration of airborne microorganisms in a DOR by about 70 percent.

(Abstract of work accomplished by Research Work Unit MR005.19-6051.)

## PATTERNS OF GINGIVITIS

*J. D. Suomi and J. P. Barbano, J Periodont 39: 71-74, Mar 1968.*

The few studies of gingivitis patterns that have been made do not indicate specific areas most and least likely to be involved. The objectives of this study, therefore, were to determine (1) which areas are most and least severely affected by gingivitis and (2) whether degrees of severity differ between corresponding right and left areas and facial and lingual surfaces of the same teeth. Subjects were 400 males,

of whom 100 were 15- to 19-year-old residents of a correctional school and 300 were inmates of a State penitentiary, each having at least 20 teeth. The latter were divided into three age groups: 20-24, 25-29, and 30-34. The gingival margins and papillae surrounding each tooth were examined and each facial and lingual aspect was scored. A score of zero was assigned for no inflammation, 1 for mild inflammation, or 2 for severe inflammation. The following observations were made: gingivitis scores increased with age; corresponding right and left areas displayed similar patterns except that scores for lingual surfaces were slightly greater for the right segment, and differences existed between facial and lingual surfaces of the same tooth. Comparison of facial surfaces revealed that upper molar areas were most inflamed and lower bicuspid areas least inflamed. Comparison of lingual surfaces revealed that lower molar areas were most inflamed and upper anterior areas least inflamed.

(Abstracted by: CDR W. C. Moffitt, DC USN.)

## LOCALIZATION OF HEMATOPOIETIC MARROW IN JAWS OF PRIMATES

*CDR D. D. Viles, DC USN, and*
*CDR R. E. Howe, DC USN.*

There has been a longstanding and continuing need for osteogenic material suitable for use in osseous defects of the jaws. The most commonly used donor sites are far removed from the oral cavity; however, in oral surgical procedures, it would be more desirable to utilize a site within the oral cavity. The purpose of this study was to localize sites of hematopoietic marrow in the jaws of primates. Specifically, it was desired to ascertain the presence and determine the volume of potential transplant marrow in the retromolar regions of the jaws of rhesus monkeys and baboons. The retromolar regions of the jaws from eight skulls were fixed in 10% formalin solution, decalcified in 45% formic acid and 20% citrate solution, and then processed and stained with hematoxylin and eosin. Histological examination of the tissues indicated that red bone marrow was present in both the maxilla and the mandible of all specimens. The total volume of red marrow in the regions studied amounted to approximately 1.5 cc. On the basis of these animal studies it was concluded that there is a source of red marrow available for transplants in the retromolar regions of the jaws. The quantity found is considered to be sufficient for many oral surgical procedures.

(Abstracted by Research Work Unit: MR005. 19-6052 by CDR D. D. Viles, DC USN, and CDR R. E. Howe, DC USN.)

## STANDARDIZATION AND GRADING OF INCISED CUTANEOUS WOUNDS

*CDR B. E. Crawford, Jr., DC USN.*

Repair and healing of experimental cutaneous wounds has been extensively studied with many attempts to predict the course of the healing wound. Corio categorized the histologic changes occurring after cutaneous incisions in pigs, and formulated a standardized grading of wound healing. The purpose of this study was to repeat Corio's procedures and relate the histologic findings to his grading standards. Incised cutaneous wounds were made on the backs of two Minnesota miniature pigs. Biopsy specimens were taken after 1, 2, 3, 7, 14, and 21 days; and tissue sections were prepared by use of the following staining procedures: hematoxylin and eosin, Masson's trichrome, Wilder's reticulum, and Alcian blue. Certain early changes associated with clotting were not categorized as being specific for any particular time. Epithelial changes, including epithelial spurs and epithelial islands, were not graded because they were seldom observed. Only histologic changes consistently seen in all sections were graded and compared to Corio's data. It was noted that epithelial inversion and epithelial union occurred in the first third (7 days) of the healing period. Fibroblastic proliferation and increased collagen content were not seen until the second third of the healing period (beginning after 1 week). After 2 weeks, progressive organization of the fibrous connective tissue and decreasing cellularity were apparent. The healing response was essentially completed after 3 weeks. These findings were in agreement with those of Corio. It was concluded that standardization and grading of normal wound healing on a time-percent basis was possible and might be of great value in the study of abnormal or delayed wound healing.

(Abstract by Research Work Unit: MR005.19-6052 by CDR B. E. Crawford, Jr., DC USN.)

# NURSE CORPS SECTION

## NURSING HISTORIES IN A NAVAL HOSPITAL

*LCDR J. S. Shaw, NC USN, Educational Coordinator, and LT M. McLaughlin, NC USN, Charge Nurse, Orthopaedic Surgical Ward, Naval Hospital, Bremerton, Washington, 98314.*

The decision to utilize nursing histories at our hospital was precipitated by several factors. Initial impetus was provided by attendance at a workshop on "Nursing Assessment: An Integrated Approach to Perception of Patient Cues," at Seattle Center.[1] This workshop, which stressed the importance of nursing histories, was attended by the Chief of Nursing Service and the Educational Coordinator from the Naval Hospital at Bremerton, Washington. Additional influence was exerted by the emphasis placed on this subject by McPhetridge[2] in a recent communication. Prior exposure to nursing histories had occurred at our February 1968 inservice meeting, when they were emphasized as a useful tool in developing more effective nursing care plans.

The subsequent inservice meeting was devoted to a report of the workshop proceedings, with emphasis on the effect of the nursing histories in improving and individualizing patient care. At this time, it was announced that the contaminated surgery ward would be used as the pilot study ward to determine the feasibility of using these aids in our hospital. This particular ward was selected because it was one of the busiest wards, and it has the most consistent staffing. This 21-bed ward contains three private rooms and 18 beds on the open ward. The great majority of patients are male Vietnam casualties from age 18 to 23. Most of the injuries are orthopaedic in nature. Any patient from Vietnam with an open wound is considered a potential source of infection and is admitted to the contaminated ward for initial observation. A few patients were transferred from other hospital wards because they had developed an infection.

The charge nurse of the selected ward constructed a nursing history form (Table I) based on the McPhetridge article and a sample form from the University of Washington. The format was adapted to our situation and was discussed with the charge nurses of the other wards. It was our goal to develop a nursing history which could be used with equal facility by medicine, surgery and neuropsychiatry. The various suggestions were incorporated, and the form was submitted for review and approval by the Chief Nurse and Educational Coordinator. After approval, approximately 50 copies were printed. It was decided to utilize these histories for all new admissions and for any patients transferred to the unit from other wards. Originally, the study was to be conducted on the unit for two weeks, after which a report with recommendation was to be submitted to the Chief Nurse. At the end of the two-week period, the decision was made to extend the study for an additional four weeks, because there had not been enough admissions for adequate evaluation.

A meeting was held with the ward personnel before the histories were begun on the selected unit. At this time, it was explained that these forms were being used as a more concise method by which information could be obtained to improve nursing care. The information obtained would be disseminated to the staff through the cardex system and patient care conferences. Ward personnel were informed that their unit had been selected as the test ward, and, if the histories were evaluated as useful tools, they would probably be utilized throughout the hospital. Initially, it was decided to take the nursing history as soon as possible after the patient's admission, dependent on his general condition. If the patient were too ill, the family could be utilized as a source of information. The staff members appeared interested in participating in a pilot study. Since they had some previous experience with patient conferences they were able to see how the questionnaire could assist in obtaining information more quickly.

The nursing history interview was conducted by the charge nurse at the patient's bedside. Attempts were made to provide an uninterrupted interval of 15 to 20 minutes, not an easy task on an open ward. The rest of the staff were informed that an interview was planned and were instructed to save nonessential questions until the interview was completed. The interview was conducted by the professional nurse, rather than other ward personnel, because it was felt that she was the trained observer who was better qualified to make interpretations and judgments of information obtained. The interview also demanded an individualized approach to all patients, including those less seriously ill.

The questionnaire investigated four areas: Social history, circumstances of the illness or injury, daily habits of living, and the present physical condition. Social history was obtained by such questions as marital history, number of children, religion, and relationship within the family group. At this time, we also inquired if visitors were expected and, if so, whether any restrictions were desired. Home location was included, due to the diversity of home locales. Home of record information aided the Red Cross in planning hospital visits for patients who would not normally have visitors.

Table I
Nursing History

1. Admission date _____ History date _____ Taken by _____
   Diagnosis _____ Date of Injury (Illness) _____
2. Circumstances of injury or referral
   Vietnam _____ Other _____
3. Previous hospitalizations
4. If previously hospitalized, list the kind of nursing activities that were
   Helpful
   Bothered you
5. Expectations regarding present hospital experience
6. Home location
7. Family Background
   Married _____ Single _____ Divorced or Separated _____ Children _____
   Relationship within family group
   Religion
8. Visitors expected? Yes _____ no _____
   Any restrictions desired?
   If yes, describe.
9. Taking any current medication
   Malaria prophylaxis (Vietnam)
   Any known allergies
10. Habits of Daily Living
    Food dislikes
    Fluid Preferences or Dislikes
    Sleep Habits Bedtime _____ Hrs. Sleep _____ Up at night _____
    When _____ Why _____ Bad dreams _____
    Defecation Frequency _____ Time of Day _____ Irregularities _____
    Any Treatment Used at Home _____ Dietary Control _____
    Last Date of Defecation _____
    Urinary Irregularities _____ Nature of _____
11. Interests, Hobbies, Pastimes
12. Vietnam Casualties or Where Applicable
    Skin Condition _____ Breakdown _____ Redness _____
    Draining Wounds _____ Pressure Areas _____
    Splints or Casts Location and Types _____
    Interfere with any Habits _____
    Any Wounds Present Location _____ What type _____
    Draining _____
    Prostheses _____
13. Other Specific Information
    (Vocabulary, Cultural Factors, Education)
14. Questions Patient asked
15. Additional Observations

Learning the circumstances of injury, especially with the Vietnam casualties, seemed to force the interview into greater depth. The interviewer queried the patient about previous hospital experiences, and asked if any type of nursing activity was regarded as particularly helpful or unpleasant. Often this question only elicited a general comment of "they treated me fine." However, occasionally, it produced quite strong feelings, especially with the patient who felt he had been teased because of the many daily activities he could not perform on account of extensive bilateral arm injuries. This alerted the staff to be especially careful in their conversation with this patient, and to offer to do things for him without his having to request assistance. In trying to ascertain patients' expectations regrading their present hospital experience, we learned how many were really not aware of the extent of their injuries, or what their physical limitations might be. This observation led to several staff conferences with the patient and doctor, at which time both patient and staff asked questions regarding the patient's physical condition. With both staff and patient more aware of the nature of the injuries, and with the goals of therapy clarified, nursing care improved and the patient had a better mental outlook.

In discovering the patient's habits of daily living, areas of food and fluid preferences and dislikes, sleep patterns, and bowel and voiding habits were covered. In discussing sleep habits, we learned the time of normal retirement, usual length of sleep, whether the patient routinely awoke at night and whether he had bad dreams. Several of the patients mentioned having nightmares and that they were apt to react in a hostile manner when awakened. In discovering bowel habits such as frequency, normal time of defecation, irregularities, and dietary control, we were able to plan more effectively for our bed patients. Because many of our patients arrived in hip spica plaster casts after having been in the air evacuation system for several days, we specifically asked the last date of defecation. Often these patients required immediate treatment. Voiding habits were also discussed, and any urological symptoms were brought to the doctor's attention. Attempts were made to discover any special hobbies or interests the patient possessed. Often, this was one of the most helpful questions posed. Actively pursuing interests of hobbies often assisted the patient in pleasantly utilizing his extensive period of hospitalization. Educational assistance was secured for several of the patients who had not completed high school and were interested in utilizing this time to obtain a general equivalency diploma. Often, immediate action could be initiated as a result of the information obtained during the interview, and this helped to assure the patient that the staff was interested in him as a person.

Next, the patient's physical condition was evaluated. Did he have any signs of skin breakdown? Were there any splints or casts present? Did the splints or casts interfere with any habits of daily living? Were any wounds present, and were they draining? At the conclusion of the form, there was a miscellaneous section where such special factors as blindness, deafness, difficulty in understanding English, or pertinent questions asked by the patient could be recorded.

Patients generally reacted in a puzzled but pleased manner. The information obtained was noted on the cardex as, e.g. "bilateral arm splints present—requires assistance with eating and bathing." In several instances, the information obtained served as a basis for the patient care conference. One elderly diabetic facing amputation of the left leg was extremely apprehensive about possible development of the same condition in his right leg. The staff discussed this aspect, and further decided to secure a sheepskin for protection, and apply lanolin cream to the skin twice daily, during which time the local circulation could be carefully evaluated. A bed cradle was also obtained.

One of the three nurses most directly involved in the project presented a report at the staff nurse meeting. This report elaborated on reasons for the nursing history, the form which was developed and the benefits realized. It also made recommendations for future use.

It must be admitted that this study was not without bias, since the nurses directly involved had previous exposure to similar projects and were strongly in favor of successfully utilizing this tool. The benefits realized fell into several areas. Information was obtained more expediently and comprehensively. This use of the history-taking interview and follow-up appeared to enhance patient-staff rapport, especially where the degree of injury would not require a significant amount of nursing care. Both immediate and long-term needs were identified, and action planned which resulted in more individualized care. Lack of patient-staff communication was often identified as a problem area, and steps were initiated to improve this. During patient care conferences, specific approaches were planned for each individual; conse-

quently, the entire staff became more involved in planning care and new viewpoints were injected. The conferences also revealed staff potential both in their perception of patient needs and in their suggestions of solutions to patient problems.

It was decided, on this particular ward, that the nursing history would be taken the second or third day following admission, rather than the first day. Usually, during the first day of admission, the patient is normally exhausted from his trip, especially if he has been air-evacuated, and very frequently he has been questioned by the admission personnel, ward personnel, medical officer, and relatives. Conducting the interview on the second or third day permitted the patient to rest, and sustained the focus of interest on him for a longer period of time. It was recommended that utilization of the nursing history be extended to four additional wards.

The Nursing History is a useful adjunct to the improvement of patient care, and has an important place in the "now" of nursing in the military hospital.

References

1. Nursing Assessment: An Integrated Approach to Perception of Cues. Workshop sponsored by the School of Nursing, Univ. of Washington, 7–9 February 1968, Seattle Center, Seattle, Wash.
2. McPhetridge, M.: Nursing History: One Means to Personalize Care. Amer J Nurs 68:68–75, 1968.

# OCCUPATIONAL MEDICINE SECTION

## AIR POLLUTION CONTROL

### PREVENTIVE MEDICINE

*Arch Environ Health 18(5): 834–838, May 1969.*

The constantly increasing contamination of our national air resource represents a major health challenge for the American people—not only today, but in the years ahead.

Air pollution is a problem of many dimensions. It has an adverse effect on the national economy, and on the individual economy of families in virtually every city and town. It aggravates disease in man and strikes heavily at forests and farmlands, at cattle and crops, at virtually every living thing. It impoverishes the quality of living of millions of our people.

Pollution's economic cost—running into the billions every year—provides more than sufficient motive within itself for restoring the quality of the air we breathe. But for all of us who are concerned with the prevention of disease, the overriding reason for controlling air pollution is because it is responsible, wholly or in substantial part, for unnecessary deaths and unnecessary illness, disability, and discomfort in this country.

The priority of public health protection in our efforts to clean up the air has been expressed by the US Surgeon General in the brief but meaningful statement that, "while cleanliness, comfort, beauty, and dignity are among our goals, the safety of people is an absolutely minimum requirement in pollution control."

While the sum of our knowledge of the health effects of air pollution is admittedly incomplete, the evidence that is available demonstrates beyond any reasonable doubt that air pollution is guilty of killing and disabling people, and that it is capable of doing far more widespread damage than it has already done.

There are, essentially, four types of evidence which link air pollution to specific health detriment. The first class of evidence comes from studies of major epidemics which have accompanied acute air pollution conditions during relatively short time periods. The most widely known of these episodes occurred in the heavily industrialized Meuse Valley of Belgium in 1930; in Donora, Pa., in 1948; in London in 1952 and 1962, and still again over the 1966 Thanksgiving weekend. On each of these occasions, deaths occurred at a higher rate than could normally be expected. During the London smog of 1952, for example, 4,000 more people died than would have been predicted.

Such occurrences are obvious, dramatic, tragic, and, thus far, fortunately rare. They merit and receive widespread publicity. But this element of drama tends to create the false impression that air pollution is a health hazard only when unusually severe weather conditions conspire to produce localized disasters. As a result, the hazards of air pollution are sometimes perceived as roughly equivalent to the likelihood of being struck by lightning.

The facts, of course, are quite otherwise. The subtler, less dramatic long-range effects of air pollu-

tion are of much more serious consequence to the population as a whole—a point that should not be obscured by the occasional episode.

From these episodes we can draw important conclusions, however. Most of those who die are persons already suffering from chronic respiratory or cardiovascular disease. Excessive pollution aggravates their preexisting condition to the point of death.

At Donora, for example, autopsies were performed on five persons, three of whom died during the episode and two who later died. Of the five, three showed acute irritative changes in the lungs, characterized by capillary dilatation, hemorrhage, edema, purulent bronchitis, and purulent bronchiolitis. A frequent diagnosis at autopsy was chronic cardiovascular disease, the existence of which antedated the episode. This opinion, based on observation of tissue change, confirmed the conclusion, previously reached on clinical grounds, that a preexisting heart disease increased the changes of serious illness and death during an air pollution episode.

The population of every city and town contains substantial numbers of individuals suffering from chronic respiratory or cardiovascular disease. It also contains many representatives of other population groups, including infants and young children, the elderly, and others, some of whom are known to become seriously ill or to die during severe pollution episodes.

Moreover, the air over most cities and towns contains the kind of ingredients that could produce another London or Donora. In other words, such disasters can certainly happen again, in the same cities or in any of hundreds of others.

Our knowledge of the health effects of air pollution has been amplified considerably through three additional types of investigations: statistical studies of past illness and death, as correlated with geographic locations and other factors associated with air pollution; epidemiological studies of death and respiratory function, as related to variations in air pollution; and laboratory studies of responses by animals, and in some cases by human beings, to exposure to various pollutants or combinations of pollutants.

Laboratory studies involving exposure of animals and, in some cases, human beings to controlled concentrations of gaseous pollutants, such as ozone and sulfur dioxide, agree generally with the results of epidemiological studies. One of the most significant investigations of this type resulted in the development of lung cancer among laboratory animals infected with influenza virus and later exposed to the inhalation of an artificial smog consisting of ozonized gasoline. Mice exposed to either influenza or ozonized gasoline singly did not develop lung cancer.

These are but a few of the highlights of health investigations carried out in the past few years. There have been many others, and, when combined with past studies on the subject, they form a considerable body of evidence suggesting that air pollution is associated with such important respiratory diseases as lung cancer, emphysema, chronic bronchitis, and asthma.

The fact is that much of the speculation and controversy about whether or not air pollution causes disease is irrelevant to the significance of air pollution as a public health hazard. We are accustomed to thinking that a disease state is brought about by a single cause—a carry-over from a period in public health history when virtually total emphasis was placed on the bacterial or viral agent which had to be present before a communicable disease could be recognized and dealt with. That there is frequently a simple association between an infectious disease agent and the acute disease reaction which it provokes was once a startling revelation. And in public health it has served medicine well and continues to serve it well. But we have learned that it is not the master key that unlocks all the secrets of disease and health. The idea that one factor is wholly responsible for any one illness is patently too simple to provide all the answers we need to deal with the chronic diseases which are on the rise today.

Chronic bronchitis, which in Great Britain is established as a specific disease entity, is a good example. It develops over a long period of time and can become crippling through a combination of many factors—air pollution, smoking, repeated and recurring bouts with infectious agents, occupational exposures—all affected, perhaps, by a hereditary predisposition. What then is the cause of chronic bronchitis? The answer is obvious. There is probably no single cause, but there is sufficient evidence that air pollution can and does contribute to its development. This is what really matters, whether we choose to consider it the cause, one of several causes, or simply a contributing factor.

It is informative to note that, to further remove the effects of smoking and occupation in studies of air pollution, epidemiological surveys of young children have been conducted in Japan, Great Britain, and British Columbia, all of which showed that children living and going to school in polluted areas had

lower pulmonary function and suffered more frequent and severe respiratory tract infections than children living in relatively unpolluted areas.

New criteria must be employed in assessing the damage of air pollution, criteria which include statistical evidence that a disease condition exists in a population, plus epidemiological evidence of the association between the disease and the environmental factor of air pollution, reinforced by laboratory demonstration that the air pollutants can produce similar diseases in experimental subjects. Ideally, all of these observations should be underlined by the ultimate demonstration that protection against air pollution will lessen or remove the severity of the disease.

The question that confronts us now is: How are we to accomplish this?

In plain terms, the best preventive medicine in dealing with the pollution of our air is the control of pollution at its major sources.

Today, through enactment of the Air Quality Act of 1967, directs the nation to control air pollution on the basis of scientific knowledege and provides the means by which this knowledge can be translated into effective social and political action. It compels us to do what we have the technology to do and gives us a mandate to develop the technology we lack.

Under provisions of the act, the initial actions toward setting the new control program in motion—the laying of the scientific foundation for control action—were assigned to the federal government. This will provide the states with the best available guidelines and tools to assist them in taking over responsibility for action at the regional level.

Initially, the Department of Health, Education, and Welfare was given the responsibility of defining the broad atmospheric areas of the Nation in which climate, meteorology, and topography, all of which influence the capacity of air to dilute and disperse pollution, are generally homogeneous.

As the next step, the department was instructed to designate specific air quality control regions on the basis of factors which suggest that a group of communities should be treated as a unit in setting and implementing air quality standards. Meteorological, topographical, social, and political considerations, and the nature and location of air pollution sources are to be considered.

The department is required to develop and publish air quality criteria for a pollutant or group of pollutants, with information on applicable available control techniques. The criteria describe known predictable effects of exposures to various concentrations of pollutants for various lengths of time and assist in developing standards of air quality which will become the goals of regional control efforts.

The accompanying technological reports identify the best methods available to control sources of the pollutants for which criteria are issued. These techniques may involve application of control equipment, changes in fuel use or industrial processes, etc. The reports also include costs of applying such techniques.

Under the act, as soon as a region is designated, and the department has published a criterion on a pollutant or a combination of pollutants, with information on related control technology, the state, or states, responsible for the designated region are on notice to develop regional standards and plans to implement them.

Under the timetable established by the Air Quality Act, affected states are given 90 days in which to notify the Secretary of Health, Education, and Welfare that they intend to set standards, 180 days to submit proposed standards for the Secretary's review, and a further 180 days to submit plans for implementation.

If the Secretary finds that the air quality standards and plans for their implementation are consistent with the criteria and related control technology, then those standards and plans take effect. If he finds that they are not consistent, he is authorized to initiate action to insure that appropriate standards and plans are established.

The Air Quality Act calls upon the governor or governors to hold public hearings in designated regions to develop air quality standards. These hearings provide a forum at which all elements making up the populace of the area—government, industry, public and private groups, and individual citizens—can make known their views on control programs to be instituted. These views will be heard and taken into consideration in program planning.

The act authorizes a broadly expanded federal program to seek, in partnership with the private sector, new answers in all our remaining areas of ignorance concerning air pollution and its control.

The act requires that special emphasis be given to research into new and improved methods to prevent and control air pollution from fuel combustion. Emphasis, for example, will be placed on the problem of sulfur oxides, which represent one of the most ubiquitous and harmful pollutants in our atmosphere today.

Another important provision of the act continues

federal standard-setting authority, by the earlier Clean Air Act of 1963, to control automotive pollution. Emphasis is placed on research into new, more effective automotive pollution control technology.

The first federal standards applicable to gasoline-powered vehicles and light trucks became effective within 1968 model year. These standards, also applicable for 1969 vehicles, required 100% control of hydrocarbons from the crankcase and, for a typical car, reduction in emissions of carbon monoxide from the tailpipe by about 55% and hydrocarbons by about 65%.

A distinguished member of the medical profession, Dr. John S. Chapman of the University of Texas, pointed out the dangers inherent in the course we have pursued when he said: The waste products of the metabolism of an industrial society can poison the medium on which it exists. Discharges of gases and solids into the atmosphere is a part of this metabolic waste. We must weigh carefully the effects of these materials not only as they apply directly to human disease, discomfort, or irritation, but also as they affect the environment on which we are dependent for survival.

The practice of medicine is becoming more and more imbued with the concept of treating the whole man, not merely his symptoms. This same concept is urgently needed in dealing with problems of environmental health. We must be oriented to the total man in his total environment, to the cumulative effects of a growing number of environmental hazards on a receptor—man—who can respond to them in an incredibly complex manner. It is not sufficient to narrow our interest to the effects of air pollution on the lungs, the effect of noise on the ear, or the effect of crowding on the psyche. We must identify the interrelationships of these and all other forms of environmental insult on man's physical and mental health, productivity, and ability to enjoy the fruits of our culture.

## TOXICITY OF COMMON HOUSEHOLD ITEMS

*Nat Clearinghouse Poison Contr Cent Bull, Mar–Apr 1969.*

There are innumerable common household items that children tend to ingest. The following list contains products that are less frequently discussed either because they are generally assumed to be common knowledge or considered unimportant in a toxicologic review. The more common inert "foreign" bodies such as coins and fishing weights have been omitted.

*Aerosol Sprays*—The most common propellents are the freons. In ordinary exposure they are harmless, but in deliberate, concentrated inhalations they have caused rapid death, possibly due to sensitization of the myocardium.

*After Shave Lotions*—Contain alcohol, water and perfume. Observe for alcohol intoxication. In a few cases, in children, ethyl alcohol has been reported to cause hypoglycemia.

*Airplane Glue*—These adhesive products are resins with a solvent to keep them fluid. The solvent is usually largely composed of toluene and not harmful unless deliberately inhaled in high concentrations as in "glue-sniffing."

*Alcohol Drinks*—The ethyl alcohol present may cause the common signs of intoxication. In a few cases, in children, it has been reported to cause hypoglycemia.

*Ball Pen Inks*—In the amounts available in ball point pen cartridges the ink is not a hazard.

*Barbecue Fluid*—The petroleum hydrocarbons may produce chemical pneumonia if aspirated into the lungs. This is very likely because of the low viscosity of the fluid.

*Bath Tub Floating Toys*—Water, water-glycerin combinations and sometimes mineral oil are found inside of these toys. Occasionally an oil with a strong kerosene odor has been reported. The latter should be suspect for producing chemical pneumonia.

*Battery (Dry Cell)*—Flashlight and pen-type batteries are not swallowed but may be bitten into by children. A conventional flashlight battery (size D) contains only 1/5 of a MLD of mercuric chloride for a child. Other ingredients would not be expected to cause harm in amounts present.

*Beer*—The ethyl alcohol present may cause the common signs of intoxication.

*Bleach* mixed with bowl cleaners or ammonia forms chlorine or chloramine gas. Both are irritating if inhaled but the latter has more transient symptoms.

*Body Conditioners*—Contain alcohol, water and perfume. Observe for alcohol intoxication. In a

few cases, in children, ethyl alcohol has been reported to cause hypoglycemia.

*Bubble Bath Soaps*—These are composed of detergents. If a child drinks it from bath water the most toxic effect expected would be vomiting.

*Candles*—Neither beeswax nor paraffin, with or without scent or color, is likely to cause symptoms.

*Caps for toy pistols*—The toxic ingredient is potassium chlorate present at approximately 4 mg/cap. The estimated MLD for a child is 4 to 5 grams of potassium chlorate which would make a roll of caps nontoxic.

*Cigarettes*—One cigarette or cigar contains a large amount of nicotine. However, the absorption of nicotine from tobacco apparently is delayed. The initially absorbed fraction causes vomiting, removing much of the tobacco from the stomach. Since nicotine is a liquid volatile alkaloid it would not be expected to be present in cigarette ash in significant amounts.

*Cigarette Lighter Fluid*—The petroleum hydrocarbons may produce chemical pneumonia if aspirated into the lungs. This is very likely because of the low viscosity of the fluid.

*Cocktails*—The ethyl alcohol present may cause the common signs of intoxication. In a few cases in children ethyl alcohol has been reported to cause hypoglycemia.

*Colognes*—Contain alcohol, water and perfume. Observe for alcohol intoxication. In a few cases, in children, ethyl alcohol has been reported to cause hypoglycemia.

*Crayons*—Those bearing the C. P. or A. P. designation are nontoxic. Do not confuse children's crayons with industrial crayons.

*Dehumidifying Packets*—Medicine bottles frequently contain small packets of moisture absorbent materials, most often dried silica gel or charcoal, and are nontoxic.

*Deodorizer Cakes*—Blocks are usually p-dichlorobenzine and less commonly naphthalene. The latter is more toxic to those with a glucose-6-phosphate dehydrogenase deficiency. Both these products should be removed from the stomach if child has eaten as much as a teaspoonful.

*Fish Bowl Additives*—These products contain chemicals used to control the amount of chlorine or to kill fungus. Since small fish tolerate these chemicals they would not be expected to be harmful to children. At the most these products might cause G. I. symptoms.

*Golf Balls*—The child who peels the ball down to its fluid core might experience an explosion of its liquid contents due to pressure. The most serious effect reported has been a mechanical injury to the eyes.

*House Plants*—There is very little information on the toxicity of most house plants. When no information can be found, we may assure that they are nontoxic in small amounts, since they are frequently ingested without reported symptoms.

*Kerosene*—The petroleum hydrocarbons may produce chemical pneumonia if aspirated into the lungs. This is very likely because of the low viscosity of the fluid.

*Lighter Fluid*—The petroleum hydrocarbons may produce chemical pneumonia if aspirated into the lungs. This is very likely because of the low viscosity of the fluid.

*Marking, indelible and special-purpose inks* must be held suspect because of the possibility that they include analine dyes or toxic solvents.

*Matches*—Less than 20 wooden or two books of paper matches do not contain enough potassium chlorate to be harmful to a child.

*Model Cement*—These adhesive products are resins with a solvent to keep them fluid. The solvent is usually largely composed of toluene and not harmful unless deliberately inhaled in high concentrations as in "glue-sniffing."

*Paint*—Toy, crib, windowsill, and wall paints are nontoxic if just a few flakes are ingested. However, repeated ingestion of outdoor paint chips may lead to serious lead poisoning.

*Pencils*—Lead and coloring pencils may be considered nontoxic. Even if they contain toxic pigments, coloring pencils ordinarily would not be ingested in toxic amounts.

*Plastic Cement*—These adhesive products are resins with a solvent to keep them fluid. The solvent is usually largely composed of toluene and not harmful unless deliberately inhaled in high concentrations as in "glue-sniffing."

*Play-doh*—This is composed of edible, digestable ingredients.

*Polaroid Pictures*—The pod that breaks to develop the picture contains a small amount (1 cc) of highly alkaline material (pH 13-14). The fluid used to coat the photograph is not harmful.

*Porous-tip ink-marking devices* (*felt tip markers*) —The Federal Hazardous Substances Act exempts

these devices providing they meet certain requirements. Therefore, the ingestion hazard is low.

*Putty*—Unless more than 2 or 3 ounces are ingested at one time there is no cause for alarm. If larger amounts are ingested there probably should be more concern for mechanical obstruction than chemical toxicity.

*Roach Tablets*—May contain a number of chemicals including arsenic and boric acid. However, the child in most cases eats only 1 or 2 and has no significant symptoms. All insecticides are labeled as to ingredients.

*Sachets*—Used in drawers or closets, they usually contain an inert or edible powder that has absorbed essential oils. There is probably more danger from a massive inhalation of the powder than from ingestion. Those containing crushed petals have not been reported to cause problems.

*Shaving Creams*—Aerosol shaving creams usually contain a soap. Most have a perfume and some have menthol and antiseptics in small amounts. The most serious symptom resulting from ingestion would be vomiting. The new "Thermal" shave creams contain 8 to 10% of sodium or potassium sulfite in the soap base with a 9% hydrogen peroxide solution in a separate compartment. These are mixed as dispensed from the container producing a controlled exothermic reaction. The resultant soap base contains about 10% of the sulfate salt and a small remainder of unreacted sulfite, but would have little toxicity.

*Silly Putty*—Is made of silicones and 1% boric acid. No problems anticipated, although there are warnings of possible obstruction if large amounts are ingested.

*Smoke Pellets for Train Sets*—These are usually supplied as capsules containing mineral oil or deodorized kerosene. If the kerosene containing pellet is chewed before swallowing, there is danger of aspiration and chemical pneumonia.

*Soaps*—Ordinary bar soaps may cause vomiting if ingested, but no other toxic effects are expected. Those bar soaps which contain antibacterial substances like hexachlorophene do not present additional hazards because of the small amounts present and the small quantities which are usually ingested.

*Teething Rings*—These usually contain water (sterility questionable) or a glycerin-water combination.

*Thermometers*—Broken glass may cut the mouth of children. The amount of mercury present is not harmful.

*Toilet Water*—Contains alcohol, water and perfume. Observe for alcohol intoxication. In a few cases, in children, ethyl alcohol has been reported to cause hypoglycemia.

*Tooth Paste*—Considered nontoxic—but those containing stannous fluoride have caused vomiting.

*Vitamins*—Liquid and chewable vitamins are not harmful in the usual size bottles. However, if they contain iron, gastrointestinal symptoms might be expected.

## MATCHES

*Nat Clearinghouse Poison Contr Cent, Nov-Dec 1968.*

By now, matches have nearly lived down their reputation for toxicity. At one time the principal components of matches were white (yellow) phosphorus, potassium chlorate, and sulfur. Instances of phosphorus poisonings, especially among workers in match factories, were not uncommon. Legislation in 1913 prohibited the use of white (yellow) phosphorus in matches, and it has been replaced by red phosphorus or by phosphorus sesquisulfide (tetraphosphorus trisulfide). The toxic effect of phosphorus sesquisulfide is negligible compared to that of white phosphorus. Red phosphorus is relatively non-toxic unless it contains the white form as an impurity. Other ingredients formerly employed were lead thiosulfate (2 to 3%) in safety matches, and antimony trisulfide (10 to 15%) in the striker surface (abrasive strip). These latter two ingredients are seldom used in matches today.

There are three types of matches in current use. They are the "strike-anywhere" large wooden kitchen match, the "strike-on-box" safety match, and the book match. Ingredients normally found in these matches are listed below:

*Strike-Anywhere Large Wooden Kitchen Matches:* Match-head ingredients are potassium chlorate about 330 mg (5 grains) per 20 matches; phosphorus sesquisulfide, about 220 mg per 20 matches; zinc oxide, dye pigment, abrasive (powdered glass or silica), and glue.

*Strike on Box Safety Matches* and *Book Matches:* Both types of matches have similar ingredients on the match head and on the striking surfaces. *Match-head materials* are potassium chlorate, 180 to 270 mg per 20 matches or 20-light book; potassium dichromate, 1 to 2.5 mg per 20 matches

or 20 light-book; sulfur 14 to 27 mg per 20 matches or 20-light book; starch, zinc oxide, infusorial earth, abrasive (ground glass, silica, flint), dye and glue.

Striking surface materials are present in only small amounts, but do contain red phosphorus, 40 to 60%; abrasive (ground glass or silica), 20 to 40%; and glue, 15 to 20%. Since most striking surfaces (abrasive strips) today are insolubilized, a child would not be able to ingest the striking surface materials by merely licking the strip, but would actually have to chew and swallow it.

It is thus seen that potassium chlorate is the only toxic ingredient of concern. The susceptibility of man to the toxic effect of chlorates varies widely, but the estimated lethal oral dose of potassium chlorate for an adult is about 30 grams or 400 mg/kg body weight. Five grams is considered a toxic dose, although death has been reported to result from the ingestion of as little as one gram by a child, and much larger amounts have been followed by recovery. It should be noted that repeated ingestion may lead to cumulative effect due to the slow excretion of the chlorate ion from the body. For a 1 or 2-year-old child, the estimated mean lethal dose would be about 4 or 5 grams of potassium chlorate.

During 1966 and 1967, the National Clearinghouse for Poison Control Centers received 657 reports of accidental ingestion involving matches. In almost all of these cases there were no symptoms reported, including very young children ingesting the head materials from as much as three 20-light books of matches, or one box of safety matches, or 20 strike-anywhere kitchen matches.

Eight (less than 2%) of the cases reported in 1966 and 1967 exhibited symptoms. Only 1 of these had symptoms other than nausea, vomiting, or abdominal pain. This was an 18-month-old who ingested 20 match-heads the first day and 10 more two days later. Burns on the mouth and fever over 101°F were reported and he was hospitalized for 3 days. It is the only 1 of the 657 cases reported requiring hospitalization, and the usually expected symptoms of vomiting and abdominal pains were not reported. Although the mouth burns might have resulted from a lighted match, this was not so stated. However, this case was the sixth largest ingestion reported in 1966-67, and potassium chlorate is cumulative in its effects.

One gram of potassium chlorate is present in about 90 (74 to 110) matches of the book match or the strike-on-box safety match type, and in about 60 to 65 large strike-anywhere kitchen matches. The estimated mean lethal dose of potassium chlorate for a young child would be contained in 4 or 5 times this number of matches.

Symptoms would not be expected to occur in children from the ingestion of the head materials from less than a full 20-light book of book-matches or 20 strike-on-box safety matches or less than 12 large-size kitchen matches. The chlorates exert a local irritant action on the gastrointestinal tract, producing nausea, vomiting, and abdominal pain.

Treatment for ingestion of a few match-heads is probably unnecessary. For large numbers of match-heads, induce emesis or perform gastric lavage, give milk or other demulcents, saline cathartic, and symptomatic treatment if signs of chlorate intoxication appear.

## "DO YOU KNOW"

*Occup Health Activities, USDHEW, Nov 1968.*

The Occupational Health Division of the Environmental Control Administration tested band members and dancers before and after a teenage rock 'n' roll dance in Batavia, Ohio. The music was so loud, the engineers found, that most of the teens tested suffered a temporary change in their hearing sensitivity. The music volume was around 115 decibels, approximately the same as that for jet aircraft noise which is considered dangerous to ground personnel and requires ear protection for long-term exposure.

## AMBULANCES NEED NOT SPEED

*Safety Rev 26(2), Apr 1969.*

The ambulance racing down the street, sirens wailing, may be doing the patient it carries more harm than good. Dr. Robert H. Kennedy, of the American College of Surgeons, called speeding ambulances a hazard to the patient, and said that speeding "practically never saved a life."

Dr. Kennedy, director of the College's Committee on Trauma, added, "Ambulance attendants should be adequately trained to judge the patient's condition and then, after immediate care has been given, travel carefully and comfortably with the patient, without careening around corners, jamming on the brakes, using the siren, or going through red lights (even if lawful)."

# EDITOR'S SECTION

## SOCIETY OF MILITARY ORTHOPEDIC SURGEONS

The Society of Military Orthopedic Surgeons (S.O.M.O.S.) meeting is to be held at the National Naval Medical Center, 22 through 24 September 1969.

Those on the West Coast who are eligible for the military airlift should contact Captain George M. Ricketson, MC USN, NH Oakland, California.

Reserve officers are invited and may apply for this meeting via their district command.

For further information, contact Captain Robert H. Brown, MC USN, Naval Hospital, Bethesda, Maryland 20014.

## THIRTEENTH ANNUAL SEMINAR ON PROPHYLAXIS AGAINST STREPTOCOCCAL INFECTIONS

The Thirteenth Annual Seminar on the Prophylaxis Against Streptococcal Infections sponsored by the Armed Forces Epidemiological Board, Committee on Prophylaxis Against Streptococcal Infections, Commission on Streptococcal and Staphylococcal Diseases, will be held at the Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D.C. 20012, on Monday and Tuesday, 6-7 October 1969.

Activities desiring to send representatives to this Seminar should submit letter request to BUMED, Attention Code 316, in accordance with SECNAV Instruction 4651.15 series as soon as possible.

## ETHIOPIAN MEDICAL CONFERENCE

The Naval Medical Research Unit No. 3, located at Cairo, United Arab Republic, participated in the Fifth Annual Medical Conference of the Ethiopian Medical Association. At the Conference, held in Addis Ababa, Ethiopia, four Naval Medical Research Unit No. 3 staff members participated actively. A paper on "Epidemic Sleeping Sickness in Ethiopia" was given by Doctor E. McConnell. LT L. L. Perine, MC USNR, spoke on "Bleeding in Louse-Borne Relapsing Fever." Doctor J. Schmidt was Chairman of a session while Doctor David Judge, MAJ USA MC, gave three papers: "On the Pathology of Louse-Borne Relapsing Fever," "Cancer in Ethiopia," and "Acute Orbital Tumors Seen in Addis Ababa." The Naval Medical Research Unit No. 3 is the only United States Medical Research facility operating in Africa.

—Research Div, BuMed.

## CURRENT CONCEPTS IN MEDICINE

On September 18th and 19th, 1969 the Internal Medicine Service of the Bethesda Naval Hospital, National Naval Medical Center, will sponsor its first course, "Current Concepts in Medicine." Directors are CAPT L. M. Fox, MC USN (FACP), Chief, Medicine Service, and CAPT W. M. Lukash, MC USN (FACP), Head, Gastroenterology Clinic and Research Branch.

The course will be particularly interesting to those interested in Internal Medicine and those who are preparing for their Boards. It will present a variety of informative papers, panel discussions, and movies on practical aspects of the diagnosis and management of clinical entities encountered in the practice of Internal Medicine: cardiology, dermatology, metabolic and endocrine, allergy and immunology, tissue bank, organ transplantation, enzymology, rheumatology, gastroenterology, hematology, and pulmonary disease.

Participants will be staff members of the various medical subspecialties at the Naval Hospital and also selected eminent guests and consultants to The Surgeon General of the Navy, from the Army, Veterans Administration, National Institutes of Health, and representative medical schools.

The Surgeon General of the Medical Corps of the U.S. Navy, VADM George M. Davis, MC USN, will deliver an address September 18.

Attendance is open to Naval Medical Officers, medical officers of the Armed Services in the Metropolitan Washington, D.C. area, and civilian internists in the community. Naval Reserve Medical Department personnel can receive retirement point credit for attendance at this meeting by certifying the dates of their attendance to the Officer in Charge, Naval Officer Record Support Activity, Naval Personnel Center, 30th and Fort Streets, Omaha, Nebraska 68111.

Advance registration for the course is required by August 27. Registration forms may be obtained by writing "Current Concepts in Medicine," Medicine Service, Naval Hospital, National Naval Medical Center, Bethesda, Maryland 20014.

## SURGEON GENERAL ANNOUNCES MAJOR CHANGES TO MEDICAL INTERN PROGRAM

VADM George M. Davis, MC USN, has announced that beginning with the training year 1970-1971 the Navy will effect some major changes to the Navy's recruiting and training methods for medical interns. In order to fully appreciate these changes, it is necessary to be informed as to the procedures that have been used in the past:

Since the beginning of the National Intern Matching Program, some 18 years ago, the Navy has procured its medical interns through the operations of that Program. Students were "matched" to the Navy and then assigned to hospitals by the Navy's Intern Selection Board. With the exception of some minor variations in 1968 and 1969, all internships were classified as "Standard Rotating" (4 months medicine, 4 months surgery, 2 months OB-GYN and 2 months pediatrics).

The Navy's Intern Program for training to begin on 1 July 1970 will open for applications on 1 September 1969. Students submitting applications for training to commence 1 July 1970 will apply only for the programs of their interest in the hospitals of their choice. They will then be "matched" directly to a specific program in a specific hospital.

Listed below are the internships that will be offered by the Navy for training to commence 1 July 1970:

| *Hospital* | *Program Director* | *Positions* | *Types Offered* |
|---|---|---|---|
| California | | | |
| Camp Pendleton Naval | J. T. Vincent | 12 | Rotating 0 |
| Oakland Naval | H. A. Sparks | 13 | Rotating 0 |
| | | 3 | Rotating 1 |
| | | 1 | Rotating 2 |
| | | 1 | Rotating 3 |
| | | 1 | Rotating 4 |
| | | 3 | Straight Med |
| | | 2 | Straight Surg |
| San Diego Naval | R. G. Fosberg | 29 | Rotating 0 |
| | | 6 | Rotating 1 |
| | | 4 | Rotating 2 |
| | | 2 | Rotating 3 |
| | | 2 | Rotating 4 |
| | | 3 | Straight Med |
| | | 2 | Straight Surg |
| Florida | | | |
| Jacksonville Naval | R. R. Gillespy, Jr. | 10 | Rotating 0 |
| Illinois | | | |
| Great Lakes Naval | R. F. Milnes | 4 | Rotating 0 |
| | | 1 | Rotating 1 |
| | | 1 | Rotating 2 |
| Maryland | | | |
| Bethesda Naval | R. J. Van Houten | 18 | Rotating 0 |
| | | 4 | Rotating 1 |
| | | 2 | Rotating 2 |
| | | 2 | Rotating 3 |
| | | 2 | Rotating 4 |
| | | 3 | Straight Med |
| | | 2 | Straight Surg |

| *Hospital* | *Program Director* | *Positions* | *Types Offered* |
|---|---|---|---|
| Massachusetts | | | |
| Chelsea | J. M. Young | 4 | Rotating 0 |
| Naval | | 1 | Rotating 1 |
| | | 1 | Rotating 2 |
| New York | | | |
| St. Albans | M. Edson | 4 | Rotating 0 |
| Naval | | 1 | Rotating 1 |
| | | 1 | Rotating 2 |
| Pennsylvania | | | |
| Philadelphia | D. E. Brown, Jr. | 8 | Rotating 0 |
| Naval | | 2 | Rotating 1 |
| | | 1 | Rotating 2 |
| | | 1 | Rotating 3 |
| | | 1 | Rotating 4 |
| | | 2 | Straight Med |
| | | 1 | Straight Surg |
| Virginia | | | |
| Portsmouth | R. T. Upton | 15 | Rotating 0 |
| Naval | | 2 | Rotating 1 |
| | | 1 | Rotating 2 |
| | | 1 | Rotating 3 |
| | | 1 | Rotating 4 |
| | | 2 | Straight Med |
| | | 1 | Straight Surg |

*Legend*

| | |
|---|---|
| Rotating 0 | 4 months medicine, 4 surgery, 4 electives |
| Rotating 1 | 6 to 8 months medicine plus electives |
| Rotating 2 | 6 to 8 months surgery, 4 months medicine (electives as time permits) |
| Rotating 3 | 6 to 8 months OB–GYN, 4 months medicine (electives as time permits) |
| Rotating 4 | 6 to 8 months pediatrics, 4 months medicine (electives as time permits) |
| Straight Medicine | 12 months medicine and sub-specialties thereof |
| Straight Surgery | 12 months surgery and sub-specialties thereof |

## POSTGRADUATE SHORT COURSES FOR MEDICAL DEPARTMENT OFFICERS SPONSORED BY THE DEPARTMENT OF THE ARMY DURING FISCAL YEAR 1970

The following postgraduate professional short courses will be conducted by the Army Medical Service during Fiscal Year 1970. Eligible Medical Corps, Dental Corps and Nurse Corps officers, are those who meet the criteria prescribed by BUMED INSTRUCTION 1520.8 Series; Manual of the Medical Department 6–130; and BUMED INSTRUCTION 1520.14 Series, respectively. Eligible Medical Service Corps officers are those who are currently assigned to billets with a direct relationship to the courses listed and should apply in accordance with BUMED INSTRUCTION 1520.12 Series. Officers desiring to attend should submit their requests in ample time to reach the Bureau at least 8 weeks prior to the convening date of the course desired. This lead time is necessary in order to comply with the Army request to return unused quotas 6 weeks in advance of the convening dates of the courses listed.

| *Courses* | *Installation* | *Date* |
|---|---|---|
| Accident Pathology | Armed Forces Institute of Pathology | 4-6 May 1970 |
| Aerospace Pathology | Armed Forces Institute of Pathology | 12-14 Nov 1969 |
| Advanced Clinical Pathology of the Oral Regions | Army Institute of Dental Research, Walter Reed Army Medical Center | 2-6 Feb 1970 |
| Application of Histochemistry to Pathology | Armed Forces Institute of Pathology | 12-16 Jan 1970 |
| AFIP Course in Oral Pathology | Armed Forces Institute of Pathology | 2-6 Mar 1970 |
| Armed Forces Institute of Pathology Lectures | Armed Forces Institute of Pathology | 30 Mar-3 Apr 1970 |
| Armed Forces Obstetrics and Gynecology (Seminar) | William Beaumont General Hospital, El Paso, Texas | 26-31 Oct 1969 |
| Current Concepts of Restorative Dentistry | Army Institute of Dental Research, Walter Reed Army Medical Center | 15-19 Sept 1969 |
| | Letterman General Hospital, San Francisco, California | 8-12 Dec 1969 |
| Forensic Dentistry | Armed Forces Institute of Pathology | 6-10 Oct 1969 |
| Geographic Pathology of Tropical and Infectious Diseases | Armed Forces Institute of Pathology | 6-10 Apr 1970 |
| Introduction to Electron Microscopy | Armed Forces Institute of Pathology | 8-12 Dec 1969 |
| James C. Kimbrough Urological Seminar | Letterman General Hospital, San Francisco, California | 27-30 Oct 1969 |
| Neuroanatomy Course for Selected Occupational and Physical Therapists | U.S. Army Medical Field Service School, Brooke Army Medical Center, Fort Sam Houston, Texas | 10-22 May 1970 |
| Neuropathology | Armed Forces Institute of Pathology | 9-13 Feb 1970 |
| Nutrition Review for Therapeutic and Research Dietitians | Walter Reed Army Institute of Research, WRAMC, Washington, D.C. | 2-6 Mar 1970 |
| Ophthalmic Pathology | Armed Forces Institute of Pathology | 15-19 Sept 1969<br>9-13 Mar 1970 |
| Oral Diagnosis and Therapeutics | Army Institute of Dental Research, Walter Reed Army Medical Center | 13-17 Apr 1970 |
| Oral Surgery | Army Institute of Dental Research, Walter Reed Army Medical Center | 12-16 Jan 1970 |
| | Letterman General Hospital, San Francisco, California | 27 Apr-1 May 1970 |
| Orthopedic Pathology | Armed Forces Institute of Pathology | 29 Sept-8 Nov 1969 |
| Otolaryngology Basic Science Course | Armed Forces Institute of Pathology | 13 Apr-22 May 1970 |
| Pathology of Nasal Adjoining Cavities | Armed Forces Institute of Pathology | 1-3 Dec 1969 |

| *Courses* | *Installation* | *Date* |
|---|---|---|
| Periodontics | Army Institute of Dental Research, Walter Reed Army Medical Center | 16-20 Mar 1970 |
| | Letterman General Hospital, San Francisco, California | 2-6 Mar 1970 |
| Present Concepts in Internal Medicine | Letterman General Hospital, San Francisco, California | 4-7 Nov 1969 |
| Preventive Dentistry | Army Institute of Dental Research, Walter Reed Army Medical Center | 6-10 Oct 1969 |
| Prosthodontics | Army Institute of Dental Research, Walter Reed Army Medical Center | 17-21 Nov 1969 |
| | Letterman General Hospital, San Francisco, California | 29 Sept-3 Oct 1969 |
| Radiologic Pathology | Armed Forces Institute of Pathology | 29 Sept-26 Nov 1969<br>2 Feb-3 Apr 1970<br>6 Apr-5 Jun 1970 |
| Social and Preventive Psychiatry | Walter Reed Army Institute of Research, WRAMC, Washington, D.C. | 26-30 Jan 1970 |
| Surgical and Orthopedic Aspects of Trauma | Brooke General Hospital, BAMC, Fort Sam Houston, Texas | 2-5 Mar 1970 |
| Symposium on Pulmonary Diseases | Fitzsimons General Hospital, Denver, Colorado | 15-19 Sept 1969 |
| Uniformed Services Pediatric Seminar | Fitzsimons General Hospital, Denver, Colorado | 2-5 Mar 1970 |
| Gary P. Wratten Surgical Symposium | Walter Reed General Hospital, WRAMC, Washington, D.C. | 5-8 Apr 1970 |

A copy of Army Circular 350, which provides detailed information on the above listed courses, will be forwarded to all Naval Hospitals.

—Training Branch, BuMed.

## FUTURE DISTRIBUTION OF MEDICAL NEWS LETTER TO BE VIA STANDARD NAVY DISTRIBUTION LIST FOR ACTIVE DUTY NAVY PERSONNEL

It is anticipated that the September edition of the *Navy Medical News Letter* will be distributed via the Standard Navy Distribution List (SNDL) vice personal addresses. This will apply only to current active duty Medical Department personnel. Other addressees will continue to receive their personally addressed copies as previously. SNDL distribution will improve out cost efficiency as well as place more copies in the hands of those who should be receiving the News Letter.

If any increase or decrease in the number of allotted copies are desired, please advise the Editor of *Navy Medical News Letter* (Code 38) Bureau of Medicine & Surgery etc. via the local Commanding Officer.

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